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VOL. II.—41ST YEAR

SYDNEY, SATURDAY, JULY 3, 1954

No. 1

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## Table of Contents.

[The Whole of the Literary Matter in THE MEDICAL JOURNAL OF AUSTRALIA is Copyright.]

ORIGINAL ARTICLES—	Page.	CORRESPONDENCE—	Page.
The Bancroft Memorial Lecture—Certain Aspects of Modern Drug Therapy, by A. J. Collins ..	1	A Note on Bronchiectasis ..	38
The Effect of "Diamox" on (Edema in Congestive Heart Failure, by B. G. Haynes and K. B. Khan ..	8	National Health (Pharmaceutical Benefits) Regulations ..	38
Hypertension: A Survey of Autopsy Findings from Patients Over and Under the Age of Forty Years, by V. J. McGovern and J. M. Greenaway ..	10	Vitamin B <sub>12</sub> in Cyanide Poisoning ..	39
Stilbestrol Inhibition of Adrenal Cortical Transplant Regeneration, by George Read ..	13	Delayed Post-Operative Recurzarization ..	39
A Splint for Use during Blood Transfusion in Infants, by Ralph D. Upton ..	14	The Practitioner and Urgent Calls ..	39
Phenylketonuria, by J. E. Cawte ..	15	Dangerous Drugs in Disguise ..	39
<b>REVIEWS—</b>		What Should the Cancer Patient be Told? ..	40
Bodily Changes in Pain, Hunger, Fear and Rage ..	19	<b>THE ROYAL AUSTRALASIAN COLLEGE OF PHYSICIANS—</b>	
Human Blood Coagulation ..	19	Sixteenth Annual Meeting ..	40
<b>NOTES ON BOOKS, CURRENT JOURNALS AND NEW APPLIANCES—</b>		Ordinary Meeting, 1954 ..	40
The Physician's Index of Australia and New Zealand ..	20	Research Fund ..	40
Sex, Society and the Individual ..	20	<b>NAVAL, MILITARY AND AIR FORCE—</b>	
World Medical Periodicals ..	20	Appointments ..	40
Medical Terms: Their Origin and Construction ..	20	<b>OBITUARY—</b>	
<b>BOOKS RECEIVED</b> ..	20	James Calvert Spence ..	41
<b>LEADING ARTICLES—</b>		<b>CONGRESS NOTES—</b>	
The Next Congress ..	21	Australasian Medical Congress (British Medical Association) ..	43
<b>CURRENT COMMENT—</b>		<b>UNIVERSITY INTELLIGENCE—</b>	
Visual Hazards of Night Driving ..	22	University of Melbourne ..	43
Treatment of Lupus Erythematosus with Mepacrine ..	23	<b>POST-GRADUATE WORK—</b>	
Interlingua ..	23	The Post-Graduate Committee in Medicine in the University of Sydney ..	43
The Treatment of Tuberculous Meningitis ..	24	<b>DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA</b> ..	43
Pernicious Anæmia and Cancer of the Stomach ..	25	<b>MEDICAL PRIZES—</b>	
<b>ABSTRACTS FROM MEDICAL LITERATURE—</b>		The Shorney Prize: A Correction ..	43
Radiology ..	26	<b>NOTICE—</b>	
Physical Therapy ..	26	Section of Preventive Medicine, Victorian Branch of the British Medical Association ..	43
Medicine ..	27	<b>PUBLIC HEALTH</b> ..	44
<b>SPECIAL ARTICLES FOR THE CLINICIAN—</b>		<b>AUSTRALIAN MEDICAL BOARD PROCEEDINGS—</b>	
CIII Trigeminal Neuralgia ..	28	New South Wales ..	44
<b>BRITISH MEDICAL ASSOCIATION NEWS—</b>		<b>NOMINATIONS AND ELECTIONS</b> ..	44
Annual Meeting ..	29	<b>DEATHS</b> ..	44
<b>MEDICAL SOCIETIES—</b>		<b>DIARY FOR THE MONTH</b> ..	44
Pædiatric Society of Victoria ..	33	<b>MEDICAL APPOINTMENTS: IMPORTANT NOTICE</b> ..	44
<b>OUT OF THE PAST</b> ..	38	<b>EDITORIAL NOTICES</b> ..	44

### The Bancroft Memorial Lecture.<sup>1</sup>

#### CERTAIN ASPECTS OF MODERN DRUG THERAPY.

By A. J. COLLINS,  
Sydney.

It is honourable to remember our distinguished forebears. To think of them with gratitude is dutiful yet praiseworthy. To perpetuate their memory is an act of devotion which sheds lustre on the past and provides enlightenment in the present. To profit from the contributions to knowledge made by a departed scientist is a feature of modern educational programmes.

The history of medicine provides the lives of great men for our contemplation. Some are remembered for their great contributions to scientific knowledge. Some abide in our minds because of their rugged personalities; others because of their methods and their determination in overcoming difficulties.

Bancroft, whom we honour tonight, is remembered for his scientific discoveries, for his scientific methods, and for his love of and interest in Nature. He was a natural scientist who sought knowledge from the phenomena around him. He viewed his environment with a questioning

and discerning eye. He read the secrets of Nature. In a new country, with little organized research to inspire him, he observed, he sought and he discovered by the determined exercise of those intellectual gifts with which he was endowed.

It is difficult to imagine any better example for the modern generation to follow, or any greater inspiration for us all, especially those who work in lonely places, with poor support in the way of established institutions or modern equipment.

Bancroft belonged to an era of keen investigation into the causes of disease, particularly disease of infectious or parasitic origin.

I believe that he would have been fascinated by the progress which has been made in the treatment of disease during the last few decades. I therefore chose a therapeutic subject as the basis of this oration. Indeed, the time seems ripe to take stock of our many new drugs and to assess their value. I am of opinion that the new therapeutic discoveries have not merely provided wonderful cures of disease hitherto incurable, but have led to new theories on the causation of disease, have stimulated fundamental research into cell metabolism, and last, but not least, have exposed important errors in the structure of our medical curricula.

I graduated forty years ago, at a time when physicians managed rather than treated illness. Their useful drugs were few, and they experienced many heart-breaks when faced with diseases which were then incurable. Frustrated

<sup>1</sup> Delivered at Brisbane on August 28, 1953.

by these difficulties, many physicians became cynical on the question of drugs. Medical historians refer to the therapeutic nihilism of the nineteenth century. This negative attitude towards treatment was still prominent up to the outbreak of World War I.

Today, with the aid of insulin, liver, sulphonamides and the bacteriostatics *et cetera*, the modern physician is a very busy and hopeful person. In fact, one would say that certain diseases, particularly the infections, are treated with more vigour than discretion.

The new remedies have appeared so rapidly that they reach circulation before their pharmacology is understood. A great example of this is cortisone, which in the United States of America was released for general use before its action was understood, its dangers realized or the indications for treatment properly defined. As a result, cortisone or ACTH has been applied to the treatment of an extraordinary number of diseases. One is almost tempted to believe that the modern physician's motto is: "when in doubt, try cortisone."

I consider that our knowledge has now reached a stage when we should not employ any new remedy, the structure and action of which we do not understand. Of the older remedies, some of course are traditional and their value has been properly assessed, though in some cases (for example, colchicine) still not understood.

It is interesting to note that the new British Pharmacopoeia has deleted 161 substances and added 63 substances. Some older practitioner will lose old friends in senega, senna, squill and *Syrupus Ferri Phosphatis Compositus*. Much more modern drugs, such as mandelic acid, acriflavine and dicoumarol have given way to better drugs.

One of the oldest of all, castor oil, remains. Lauder Brunton devoted half a page of his book on "The Action of Medicines" to describing how castor oil should be taken with water and brandy. The ancient Egyptians chewed castor oil seeds and drank beer, so perhaps they knew as much about the subject of disguising nasty tastes as we do. A study of the new pharmacopoeia emphasizes what we all know—that prescribing in future will be restricted considerably to single substances rather than compound medicines.

A prominent pharmacist recently defended the prescribing habits of certain doctors by saying that a doctor needs to be a psychologist. With this I have no quarrel; but I maintain stoutly that psychological effects should be obtained by rational explanation. (The prescribing of inert or useless mixtures with the intention of producing a psychological effect cannot be too strongly condemned. Fortunately the medical profession has risen superior to this shabby device.)

Drugs should be and are now used for their predictable and desirable pharmacological effects. The modern generation of doctors, for the most part, does not believe in bluffing the patient. In the days gone by, when the causes of diseases were unknown, these diseases were treated empirically and symptomatically. Some of the remedies used by physicians in the middle ages were disgusting, whereas the foundations of surgery were being laid simply, tentatively, but with promise.

Ambroise Paré, the sixteenth century military surgeon, was a man of scientific tendencies. The famous saying "I dressed him, and God healed him" was his devout tribute to the deity and to the *vis medicatrix naturæ*.

By contrast, the physician of the period, after giving one of his foul messes to a patient, might justly have said: "I dose him, but God help him."

There were, of course, traditional drugs of such value that we still use them. Quinine is an interesting example coming from South American folk medicine into Spanish medicine. The likeable story that cinchona derived its name from a Spanish countess who was cured by it has been disproved. The facts are, however, that the value of cinchona was recognized by the Spanish invaders of South America. It was for years known as Jesuit's bark. In an age of religious persecution it can be said that their bark was preferable to their bite.

To illustrate the futility of medical treatment during the reign of Charles I, I show a prescription recommended for plague by the Royal College of Physicians in 1636.<sup>1</sup>

Take the shavings of Harts horne, of Pearle, of Corall, Tormentill rootes, Zedoarie true Terra Sigillata, of each one dram, Citron pills, yellow, white and red Sanders, of each halfe a dram, white Amber, Hyacinth stone prepared, of each two Scruples, Bezoar stone, of the East Unicorne's horne, of each 24. graines, Citron and Orange pills candied, of each three drams, Lignum Aloes one scruple, White Sugar Candie, twice the weight of all the rest, mixe them well being made into a powder. Take the weight of 12d. at a time every morning fasting, and also in the evening about five a clocke or an houre before supper.<sup>2</sup>

The College which was responsible for the effort fled from London during the Great Plague. How far we have gone since those days! There is a reasonable prospect of cure even of pneumonic plague if bacteriostatics can be given early.

The outstanding victories of the last thirty years in the field of therapeutics have been gained by insulin in diabetes, by liver in pernicious and similar anæmias, and by the bacteriostatic drugs in infectious disease (including venereal disease).

Less definite, but of tremendous value, have been the use of thiouracil in hyperthyroidism and finally that of cortisone and ACTH in rheumatic disease and certain other conditions.

#### Liver Therapy.

I propose to discuss certain aspects of modern therapy and will commence with liver therapy in pernicious anæmia.

When the cause of a disease has been discovered, purposive research to find a cure is thereby stimulated. In the case of pernicious anæmia the reverse is true. Actually the discovery of controlling treatment has led us far towards discovering the cause of this complaint. The story is a fascinating one.

Liver is a substance which has long been valued for nutritive purposes. Primitive people were well aware of its value in this connexion. We read of the Red Indians of North America using liver as a food for people who have been found suffering from exposure and starvation. It was not till a quarter of a century ago that Minot and Murphy startled the medical world with proof that liver could reverse a relapse in pernicious anæmia and maintain a normal blood count if given indefinitely at suitable intervals. Thus was pernicious anæmia demonstrated to be a deficiency disease. The liver was at first given orally in a raw or partly cooked state. It was but natural that fluid extracts for oral and subsequently parenteral use should in due course be provided.

The parenteral use of some of the cruder extracts affected some patients with allergic phenomena of the usual type. More refined extracts followed, and it was found that whilst the finer extracts were much more potent and relieved us of a danger of allergic reactions, the cruder extracts were of more value in treating neurological complications of pernicious anæmia. Soon after Minot and Murphy made their discovery a study of bone marrow threw interesting light on pernicious anæmia and similar blood conditions. It was found that there was a megaloblastic reaction in the bone marrow, not only in pernicious anæmia, but also in the pernicious-like anæmias of sprue, certain nutritional deficiencies and pregnancy. Furthermore, Castle's work indicated that the hematopoietic principle lacking in the pernicious anæmia-like conditions could be provided by a combination of an extrinsic factor ingested in certain foods and an intrinsic factor found in the stomach of normal people. In Addisonian anæmia the intrinsic factor was lacking.

<sup>1</sup>One of the many prescriptions for treatment of the plague supplied by the Royal College of Physicians of London by "his Majesties speciale Command", 1636. From "Certain Necessary Directions, as well for the cure of the Plague, as for preventing the infection . . .", London, 1636.

<sup>2</sup>Zedoarie, aromatic Oriental root; Sanders, sandalwood; Bezoar, concretion from animal stomach or intestine.

In some other conditions delayed absorption of the combined product was responsible for the megaloblastic anaemia (for example, in sprue) and in others (for example, nutritional anaemia) the delayed absorption was responsible. However produced, the anti-anaemic principle, as it is now called, is stored in the liver. Another chapter in this fascinating story of the megaloblastic anaemias begins when the Merck Laboratories produced vitamin  $B_{12}$  five years ago. Sufficient time has elapsed to prove that vitamin  $B_{12}$  can do all for pernicious anaemia that has previously been done by liver. It certainly does appear that the efficacy of liver in pernicious anaemia was due to its vitamin  $B_{12}$  content.

There is no doubt that vitamin  $B_{12}$  will replace liver in the treatment of this disease, and in fact in many clinics it has already done so. It can be administered orally, but its parenteral use is more economical and more satisfactory. Most importantly, it relieves non-reversible neurological complications. Orally, vitamin  $B_{12}$  must be given in doses forty times larger than the dose for parenteral use. The absorption is uncertain, but does occur by mass action. There is no doubt now that vitamin  $B_{12}$  was absorbed by mass action in early days of liver therapy when large amounts of liver meat were taken; but the interesting point is that its absorption is facilitated after incubation with normal gastric juice.

Our experiences with vitamin  $B_{12}$  have led to a widespread belief that it is the anti-pernicious anaemia principle itself. Thus our conception of the causation of pernicious anaemia has been recast. The role of the intrinsic factor is believed to be mainly to facilitate absorption of vitamin  $B_{12}$  from food, possibly, as Goodwood has suggested, by freeing it from a conjugated form. This simple theory does not explain all the problems involved, and it is not my purpose to review these problems. I do wish to emphasize that the discovery of vitamin  $B_{12}$  has done far more than provide the most satisfactory treatment of pernicious anaemia. It has focused to a fine point interest in the maturation of red cells and the aetiology of the megaloblastic anaemias.

Before discussing the treatment of the non-Addisonian megaloblastic anaemias, let us consider the position of folic acid. In 1945 folic acid was obtained from liver and later synthesized as pteroyl glutamic acid. It was found to be effective orally as well as parenterally in relieving pernicious anaemia in relapse, and other megaloblastic anaemias. Its effects in pernicious anaemia were variable on the blood picture and absent on the neurological complications. Indeed, in some patients the latter were intensified, so much so that its use in pernicious anaemia was abandoned. However, it was found effective in refractory pernicious-like anaemia and in non-Addisonian megaloblastic anaemias. The relationship of vitamin  $B_{12}$  to folic acid is undergoing investigation and is the subject of many theories. It has been discovered that there is a third principle in liver, folinic acid. This is probably an active form of folic acid. One theory is that folinic acid is necessary for the maturation of megaloblasts and that vitamin  $B_{12}$  is necessary to convert folic acid into folinic acid. The subject is very confused, but the results of treatment are plain.

The position today is that pernicious anaemia in relapse can be effectively treated by crude or refined liver extracts or by vitamin  $B_{12}$ . It is believed that liver acts in this disease only by virtue of its vitamin  $B_{12}$  content. Therefore liver is no longer necessary for pernicious anaemia. The non-Addisonian megaloblastic anaemias are treated effectively by crude liver extracts or by folic acid, but not by refined liver extracts or by vitamin  $B_{12}$ . There is reason to believe that the crude liver extracts act solely because of their folic acid content. (The action of vitamin  $B_{12}$  is to help maturation of red cells. The action of folic acid is not properly understood.) It would appear, therefore, that with vitamin  $B_{12}$  and folic acid available we no longer need liver extracts. The first can be used for pernicious anaemias and the second for the non-Addisonian megaloblastic anaemias.

It cannot be too strongly emphasized that the only anaemias for which liver is valuable are the megaloblastic anaemias. Its use for normoblastic iron-deficiency anaemias has no pharmacological sanction. Inasmuch as these two new substances can provide better results in their appropriate therapeutic fields than crude or refined liver extracts, it is not to be wondered that pharmacologists consider that liver extract will soon be replaced. One can, almost with certainty, I believe, dispense with the refined extracts. There is a lingering fear that there may still be some unknown anti-anaemic substance of importance in crude liver awaiting discovery. For this reason we hesitate to give firm advice about excluding crude liver extracts from our pharmacopoeias at this juncture. It is interesting to note that after vitamin  $B_{12}$  was discovered, an assay of existing liver extracts for vitamin  $B_{12}$  gave surprisingly low figures in some instances. Manufacturers are now adding vitamin  $B_{12}$  to their liver extracts to make sure of their therapeutic potency. In some cases they are adding more than is needed. It is generally conceded that 50 microgrammes per fortnight would be a maximum maintenance dose. Some liver extracts now are advertised to contain 100 microgrammes per cubic centimetre.

The well-known toxic effects of liver—namely, urticaria and other forms of dermatitis, fever, substernal oppression, hypotension, flushing and abdominal pain—are not a feature of vitamin  $B_{12}$  therapy.

Lastly, there is now available for oral use a preparation of vitamin  $B_{12}$  and intrinsic factor combined—for example, "Bifactor" (Organon). Thus we seem likely to go right round the clock, from the early oral liver meals and liver extracts to the oral use of the essential anti-anaemic principle along with the factor essential for its absorption.

#### The Treatment of Diseases of the Heart.

Digitalis has been in use for over two hundred years. The country folk of Shropshire used a decoction of foxglove for dropsy. In 1785, four years before the outbreak of the French Revolution, Withering published his "Account of Foxglove".

At the turn of the present century its action was imperfectly understood and its application was of necessity restricted. With MacKenzie's work on auricular fibrillation the correct control of this condition by digitalis was established, even though to this very day the mode of action and the particular pharmacological response for which we have to thank digitalis in the relief of congestive heart failure in general, and auricular fibrillation in particular, are still the objects of active investigation.

Although these investigations throw new light on old problems, the treatment of auricular fibrillation and auricular flutter by digitalis is little different from that of MacKenzie's day. Today massive doses of digitalis are employed, as against the slower method of digitalization employed in my student days. Furthermore, the tincture of digitalis has disappeared from the modern therapeutic armamentarium and has been replaced by digoxin or digitoxin. The tincture varied in its therapeutic quality and was standardized by biological assay. It contained, in addition to the useful glycoside, saponins which were responsible for more nausea and vomiting than follow the use of the more modern preparations. Digitoxin is very potent and very toxic. It has the advantage that a single dose of 1.2 milligrammes will digitalize a heart fully. It is completely absorbed from the stomach, so that intravenous use has no advantage over oral use. But in British communities digoxin is the preparation most used. It is a crystalline glycoside standardized by weight—a great advantage.

I wish to refer specially, however, to the use of quinidine to restore rhythm in auricular fibrillation. Parkinson taught that this drug, which is absorbed and utilized within two hours, should be given in two-hourly doses up to a maximum of 30 grains daily. He laid down certain conditions for and contraindications against its use. The heart should be digitalized before quinidine is given, and its use should be prohibited in the treatment of patients with congestive failure, valvular disease, very large hearts,

and fibrillation of longer duration than six to twelve months. The danger of embolism prompted these precautions. In a recent review of the value of quinidine therapy in auricular fibrillation, Weisman (1953) holds that doses of more than 30 grains daily are dangerous because of the risk of asystole. He reminds us that quinidine is a highly potent drug, a cardiac depressant. It depresses the sino-auricular node and increases the auriculo-ventricular and intraventricular conduction time. In toxic doses it may cause asystole, and overdosage may cause respiratory paralysis. The point to be determined, of course, is what are toxic doses. It is definite that the conventional dosage of 30 grains a day frequently fails to restore normal rhythm.

Prinzmetal states that this failure will be observed when the ectopic focus is stronger than the sino-auricular node; whilst Lewis explained such failure by a greater action of quinidine upon the conduction rate of circus movement than upon the refractory period of the heart. The subject is a difficult one. Examination of the level of quinidine in the blood has not helped in determining dosages. Restoration of normal rhythm has been noted in patients with such low blood levels as four milligrammes of quinidine per litre or less, and not with much higher levels. As is well known, quinidine is readily absorbed and rapidly excreted, which would render difficult the maintenance of an even level of the drug in the blood. There is no need, therefore, to rely on blood estimation for this purpose.

There is reason to believe now that we have been too cautious in the use of quinidine. There can be no question that quinidine should be used to restore rhythm to normal in established cases of auricular fibrillation. Ample evidence has accumulated to indicate that cardiac efficiency is greater, other factors being equal, if this rhythm is normal.

Goldman and others have used quinidine in the treatment of patients with very large hearts, and have noted that the size of the heart diminished with the establishment of normal rhythm. They have used it in congestive heart failure and in the treatment of patients with valvular disease. They have used it with digitalis simultaneously and have employed much larger doses than the 30 grains a day previously laid down. The patients in whom brilliant results have been obtained are those who are invalided with large fibrillating hearts and congestive failure. The restoration of normal rhythm has cleared up congestion and reduced the size of the heart, and these patients have been able to leave their beds and lead more useful lives.

The danger of embolism, which used to be emphasized in regard to quinidine therapy, and which was the basis upon which rested the pronounced contraindications to quinidine therapy mentioned above, would now appear to be greater in untreated patients than in those who have been given quinidine, even late in the disease, and in the presence of congestive failure. Probably a correct procedure would be to treat all patients in bed and to digitalize them first. Whether digitalis therapy should be suspended or not during the first quinidine trial does not seem to matter. If congestion is only partly relieved by full digitalization, this should not deter us. Quinidine should then be administered gradually, after a test dose in amounts up to a maximum of 30 grains daily. Failure after one week should be followed by one week's rest, after which a second attempt may be made. A second failure may be followed by a cautious increase of the dose. It is noteworthy that in many patients reported as having required unusually high doses of quinidine to restore normal rhythm, relapse has occurred early in spite of the exhibition of maintenance doses.

Quinidine also has a useful function in the treatment and prevention of paroxysmal tachycardia, and in the prevention of paroxysmal auricular fibrillation and flutter. The new treatment of paroxysmal ventricular fibrillation by "Pronestyl"—a procaine amide—is deserving of close attention. This drug has considerable hypotensive tendencies and its use can be dangerous. For this reason the intramuscular route seems preferable to the intra-

venous route of administration, the dose being 0.5 to 1.0 gramme every six hours. Its greatest value should be in treating prolonged bouts of ventricular tachycardia, especially after a coronary occlusion.

When Lauder Brunton introduced nitrites for use in treating angina, he conferred great benefit upon invalids. (Nitrites act by virtue of the O-N-O group, which relaxes plain muscle and causes vasodilatation.) Dilatation of the coronary arteries increases blood flow. Dilatation of peripheral vessels lowers the blood pressure and decreases the load upon the labouring heart. It will doubtless interest the young men of my audience to hear that Lauder Brunton discovered this effect of the nitrites and applied this knowledge to relieving angina of effort during his term as a house doctor. Little concentrated investigation of these drugs has been made since the work of Evans and Hoyle, published nineteen years ago. They investigated all the nitrites and tested their stability. It is important to know that amyl nitrite in capsules remains stable for many years. On the other hand, glyceryl trinitrate tablets do not keep well unless specially coated. Glyceryl trinitrate—a nitrate—is converted into nitrites in the body after absorption. Its action is powerful and it is preferred to the other nitrites because of its rapid predictable action. Sodium nitrite, erythrol tetranitrate and the new drug pränitron are gentler, slower and more prolonged in their action. Sodium nitrite has been deleted from the last British Pharmacopœia. The whole point about angina of effort is that it is an emergency requiring prompt action. Glyceryl trinitrate in the relief of this emergency provides the quick and certain action required, and must be preferred.

When the exhibition of nitrites is required to prevent pain, and when they are taken for this purpose before some routine activity which is known otherwise to produce pain, it seems more logical to use a more slowly acting drug which has a more prolonged pharmacological effect. Notwithstanding this *a priori* reasoning, it is observed in practice that glyceryl trinitrate is an admirable drug to prevent pain which without it would be bound to occur.

I need not remind the physicians in my audience that there are other ways of preventing angina than by drug treatment.

Finally, with so-called angina decubitus, to counter which it is common practice to administer a drug hourly or two-hourly as a preventive, once again a drug like pränitron should be preferred because of its longer effectiveness. The various surgical treatments of angina by injecting alcohol or by cutting nerves could in some cases be avoided by greater care with and study of the individual reaction to nitrites.

Papaverine, a benzoyl-isoquinoline alkaloid of opium, is a useful drug. It relaxes tone or spasm of all smooth muscles, but does not interfere with normal peristalsis (Salter). It depresses cardiac action by its effect on the myocardium and conducting tissues. In coronary disease it is used to increase coronary flow, especially after cardiac infarction with the associated coronary spasm.

Theophylline, like the other xanthines caffeine and theobromine, has a vasodilator effect. It is more useful than the other xanthines. It is frequently given as aminophyllin, in which it is combined with ethylene diamine so as to promote its solubility to 1 in 5 from 1 in 160, and therefore provide more rapidity of action.

It is interesting to note that in the case of glyceryl trinitrate the action occurs within from one to four minutes and has passed off within ten minutes.

In the case of erythrol tetranitrate and mannitol hexonitrate the onset of action is noted within fifteen to thirty minutes and the duration of action is over three to six hours. Theoretically the latter should be preferable to nitroglycerine as a preventive of angina. However, practical experience has shown that in 50% of people the action is very poor, possibly owing to destruction in the intestines. Furthermore, tolerance is established against the slowly acting nitrates, which is not the case with those which do not remain long within the body. This is a most

important fact which must be borne in mind in treating established angina.

The nitrites produce these pronounced effects upon angina largely by lowering the peripheral resistance. Papaverine and aminophyllin, which are not used to relieve angina as a routine treatment, but are reserved for (a) the angina following infarction and (b) paroxysmal nocturnal dyspnoea, are successful because their effect upon the coronary vessels is more pronounced than their peripheral effects. McMichael, however, considers that the relief of Cheyne-Stokes breathing following treatment with aminophyllin is due to the ethylene diamine content of the drug and not to the theophyllin. He considers that ethylene diamine stimulates the respiratory centre. Clearly, more research is needed upon the pharmacology of the vasodilators.

With so many vasodilator drugs at our disposal it is disappointing that we have not met with great success in the drug treatment of peripheral vascular disease.

Goodwin (1951-1952) summarizes his view on the pharmacological approach to the medical treatment of peripheral vascular disease. He refers to the newer compounds, whose action depends (i) upon blockade of the autonomic ganglia, sympathetic constrictor impulses being thereby inhibited (for example, tetraethyl ammonium salts, methonium compounds), (ii) upon adrenergic or sympatholytic properties, or (iii) upon specific local action upon the vessel walls (for example, "Dibenamine"). The great disadvantage of the first group is that they are not selective in their action, and their action is only temporary. They dilate all the peripheral vessels and therefore do not increase the quantity of blood available for the ischemic part.

Goodwin considers the imazolin compound "Prisol" the best of a poor lot. Its action is in a partly adrenergic, partly sympathomimetic antipressor direction, and partly directly antispasmodic on the vessel wall (25 to 100 milligrammes are given thrice daily). It has more effect upon skin vessels than upon the larger arteries supplying muscles. Its side-effects are few and comparatively innocuous (headaches, giddiness, goose flesh). Goodwin also discusses "Hydergine", a hydrogenated ergot preparation. By hydrogenation the ergot alkaloids are deprived of their vasoconstrictor properties. "Hydergine" is a combination of three of these alkaloids (dihydroergocryptine, dihydroergocristine and dihydroergocornine). Both these drugs can be given by mouth for long periods.

There is no question that sympathectomy is the best treatment offering for these chronic and progressive arterial diseases. It is more immediately effective than any drug, it is selective as to the site of action, and it is more permanent. Naturally it is not resorted to unless the occlusive process reaches a critical point.

Pickering and Waine have reemphasized a matter of which physicians have been aware for years—namely, that anaemia aggravates occlusive arterial disease. In coronary disease or peripheral vascular disease one must consider the quality of the blood when it is quantitatively reduced. If the oxygen-carrying power of the blood is reduced, it is logical to correct this defect as an essential part of treatment.

#### Modern Therapy and Medical Education.

The advances of organic chemistry are influencing drug therapy so rapidly that the medical profession is becoming bewildered. Doctors are being called on to prescribe drugs of complex formulae, the comprehension of which is beyond their chemical knowledge—bearing long names which are so difficult that they must perforce be shortened into official names, which, like the names of racehorses, are supposed to yield some hint of their origin.

The important fact revealed is that the medical profession has not had sufficient fundamental instruction in chemistry and physics to keep abreast of the new knowledge. In so far as the present generation is concerned, nothing can be done about it. It is sincerely to be hoped, however, that medical students in the future will be

encouraged to spend more than one year studying the basic sciences. Ideally, a degree in science should be a necessary preliminary to a medical course. Alternatively, medical students might be recruited from the ranks of science graduates. At the present time, physiology and pharmacology are being taught and investigated by science graduates in increasing numbers. Many chairs in their subjects are held by science graduates, whereas once they were mainly occupied by medical graduates. Every medical school should have a chair in pharmacology and facilities for research in this subject.

There can be no question that the scientific pharmacologist would be better with medical knowledge, just as the physician would be better with increased knowledge of the basic sciences. The quality of the graduates of a particular university must be related to the attention which that university pays to the basic sciences.

Overseas next month a conference upon medical education is taking place in Europe. A great and most serious problem has arisen for those who plan medical curricula; for the fact is, paradoxically speaking, that our new knowledge has brought to light our gross ignorance.

#### The Anti-Histamine Drugs.

The foregoing remarks have particular reference to the so-called antihistamine group of drugs, concerning which I propose to address a few remarks to you.

This large group of new drugs is of great interest and deserves study. There can be no question that they have captured the imagination of a profession which is yearning to do something positive in the treatment of diseases which have hitherto proved difficult, like hay fever, asthma *et cetera*, as well as a host of minor manifestations of allergy. The result has been an uncritical and widespread use of drugs which are imperfectly understood and ill-applied.

During the closing phases of World War I, Dale, who had already reported upon the similarity between histamine shock and anaphylaxis, suggested that traumatic shock, which had been such a serious complication of war wounds, was due to the release of histamine. Lewis and his co-workers studied the results of applying histamine to the scratched skin, and described the triple response of preliminary pallor, followed by redness and infiltration. They suggested that allergic phenomena, because of their similarity, might be due to the liberation of an H substance closely resembling histamine. It is known that histamine is widely distributed in the body. It is especially well represented in the lungs and leucocytes. It is bound to protein. It is released by injury or by hydrolysis, whether by acids or enzymes or bacterial action (Salter).

The action of histamine is to contract smooth muscle and to dilate the peripheral small vessels. It also stimulates the action of most glands (for example, the acid-secreting glands of the stomach). Gaddum emphasized how little we know about histamine. He stated that there was enough histamine in a cat to kill it, but that we did not know why normally it did not do so.

Dale distinguished between intrinsic histamine, which is released by cells giving the response, and extrinsic histamine, which is released by one cell and acts upon another. Released or injected histamine rapidly disappears from the blood and is taken up by various tissues in which it is rapidly inactivated. The enzyme histaminase plays an important part in this process of destroying histamine. It exists in most tissues according to Gaddum; but Salter states that it is absent from the skin, heart and stomach. A deficiency in histaminase may be a causative factor of allergic diseases. Gaddum suggests that a deficiency of histaminase in certain tissues may account for the localization of allergic phenomena—for example, the skin in urticaria, the nose in hay fever, and the lungs in asthma.

With these preliminary remarks about histamine we are in a position to discuss the antihistamine group of drugs.

In the last five years these drugs have been widely used. More and more are being manufactured. They are all synthetic organic compounds, many bearing two or

three names. Certainly, as someone has pointed out, there are far more names than drugs, which is very confusing to the practising doctor. Nevertheless their chemical structures are not unlike, being substituted amines. Salter gives the following classification. Group I:  $R-O-CH_2CH_2N(CH_3)_2$ , diphenhydramine hydrochloride ("Benadryl"), dimenhydrinate ("Dramamine"); Group II:  $R-N-CH_2CH_2N(CH_3)_2$ , pyranisamine maleate ("Neo-Antergan"), thonzylamine hydrochloride ("Neo-hetramine") *et cetera*; Group III:  $R-CH_2CH_2CH_2(CH_3)_2$ , propen pyridamine maleate ("Trinetron").

These drugs have been found to have an antihistamine action upon the experimental animal. They do not counteract the pharmacological action of histamines, as does adrenaline, but rather block the effective union of histamine with the cell receptors (similarly to the action of atropine in blocking acetylcholine). They can prevent the development of anaphylaxis in a sensitized animal, the development of asthma from histamine inhalation, and the development of skin reactions. When they are applied to the treatment of human beings, their results have not been so striking. They have a low therapeutic index, toxic symptoms developing in a moderately high proportion of patients treated. These are drowsiness, headaches, dizziness, nausea, weakness and mental confusion. Patients undergoing treatment are warned against driving a motor vehicle or handling dangerous machinery. The drugs are absorbed readily by mouth, but are excreted rapidly, their period of effective action being but a few hours. The parenteral use of antihistamines is therefore not recommended for any condition in which long action is required. They have little beneficial action on most asthmatics. Their greatest value seems to be with seasonal hay fever and the skin manifestation of allergy. Dale suggests that their action is likely to be confined to countering extrinsic rather than intrinsic histamine. Among the first of these drugs to be used was "Benadryl". Another early one was tripeleminamine hydrochloride ("Pyribenzamine"). Others are "Antergan", "Antistine" and "Theophorin", and amongst the newer ones "Ambodryl", propenpyridamine maleate and thonzylamine hydrochloride ("Neo-hetramine").

The early enthusiasm of drug-hungry allergists has been dampened by disappointing or, at the most, moderately successful results. It must be remembered that these drugs do not prevent the release of histamine, they merely prevent histamine from combining with cell receptors in the affected tissues. Furthermore, it is probable that histamine is not the only toxic substance released by damaged cells. Animal experiments seldom apply completely to human beings. Allergic people differ considerably in their reaction to the same allergen. There are three variables to be considered: (i) the amount of histamine to be blocked; (ii) the patient's sensitivity to histamine; (iii) the patient's deficiency of histaminase.

One may postulate the greatest success for antihistamine in a very sensitive patient who reacts violently to a small release of histamine. If, in addition to these two conditions, it is postulated that the histaminase deficiency is small, the antihistamine effect of appropriate drugs would be even greater. One useful action of antihistamines is to prevent allergic reaction to other drugs—for example, penicillin, streptomycin and sulphonamides—in sensitive patients. Another is the prevention of seasickness and airsickness. "Dramamine" (dimenhydrinate) is used for this purpose; it inhibits vomiting. "Dramamine" is a chlorotheophylline salt of diphenhydramine which is equally as effective, so it is said, as hyoscine.

Unfortunately, antihistamine drugs are often administered unwisely—for example, to patients with a cold in the head or with recurring coryza—in the belief that they have hay fever *et cetera*. Failure to distinguish between recurring infection and true allergy has brought undeserved disrepute upon antihistamines. These drugs are being produced too rapidly for our mental digestion. My advice to the profession is to learn their pharmacological action from the scientific journals and not from

the beautifully illustrated and expensive advertisements and books published by the big drug houses.

The newer antihistamines are not so well understood as "Benadryl", "Pyribenzamine", "Antistine" and "Neo-antergan", to mention a few. It may be said, however, that until we obtain drugs which have a longer action and a higher therapeutic index than those which have had long trial, we are not likely to make more satisfactory progress in treating allergic diseases.

Finally, it is somewhat disturbing to realize that there is some evidence, certainly not well substantiated, that a few patients have become allergic to antihistamines.

#### The Bacteriostatic Drugs.

There is no need for me to refer to the revolution in the treatment of pneumococcal and streptococcal diseases by the sulphonamides. Their probable mode of action has been explained and their toxic effects are well known. The great importance of using these drugs has been the development of a new technique, that of checking results by the blood concentration, and of thence arriving at the optimum blood concentration for a particular complaint. This has eliminated guesswork in dosage. The much more valuable antibiotics, which became available with penicillin *et cetera*, led to the control of diseases like infective endocarditis, which had defied all our previous efforts. The wide range of organisms vulnerable to the different antibiotics were studied and the new phenomena of drug sensitivity and drug resistance on the part of organisms came under our notice.

I propose to say something of the mode of action and toxic effects of these drugs.

Penicillin is still a very important drug. Some physicians thought a few years ago that penicillin was likely to be abandoned. They were far from correct. As a matter of fact, it is still perhaps the most useful of the antibiotics. It is important, therefore, that its toxic effects should be well understood. These are general and local reactions. Sudden shock may occur after a first injection and may even result in death. The phenomenon of natural hypersensitivity is often incorrectly described as anaphylaxis. Anaphylaxis is an acquired condition occurring most frequently when a second course is instituted, ten days or more after a first course of penicillin has been administered. These patients develop shock, a rapid pulse rate and a lowered blood pressure. Some doubt has been expressed lately with regard to some of these cases of shock which followed intramuscular injection of procaine penicillin. It has been suggested that the shock was due to procaine poisoning. I think this is exceedingly unlikely, as procaine is not a toxic drug. There is from 37.5% to 40.5% of procaine in procaine penicillin and the required dose will be contained in one cubic centimetre. It is possible, however, that a procaine idiosyncrasy rather than procaine poisoning may be the cause. The local effects are seen in the skin, and consist of urticaria, giant urticaria, purpura and irritative dermatitis of varying grades. Fever is fairly common after penicillin has been given.

It would be a counsel of perfection to advise skin testing before penicillin is administered. It is, however, a wise course to test skin sensitivity for penicillin when giving second courses at an interval after a first course. An intradermal injection of a solution of 1000 units in one cubic centimetre of water will suffice.

It has been reported that a Herxheimer reaction may result from giving penicillin to syphilitic patients. This is not well authenticated. On the contrary, late clinical reports indicate that patients with cardiac syphilis can be treated without fear of such a focal reaction without the preliminary protection of bismuth or iodides.

Streptomycin causes similar allergic skin reactions to penicillin. It also causes histamine-like shock, as in penicillin collapse. This is rare with the pure preparations of the drug.

Specific affections of the central nervous system are seen in the shape of dizziness, vertigo and tinnitus due to an eighth-nerve affection. These results occur after two weeks

of therapy. They may be prevented by giving small doses at longer intervals (for example, one gramme twice a week) when tuberculosis is treated in the ideal way by combining INH or PAS with streptomycin, in accordance with modern practice. This régime may be kept up for months without toxic effects.

Streptomycin resistance also is not so likely to occur in such combined therapy.

The toxic effects of aureomycin are mild and are referred to the alimentary tract. Chloramphenicol, however, has caused agranulocytosis and should be used with caution.

The mode of action of antibiotics is imperfectly understood, but is being closely investigated. A symposium upon the subject was recently published in *Bacteriological Reviews*, by Wyse, Small, Hoblig, Oginsky and Pratt. Pratt pointed out that penicillin caused bacteria *in vitro* to swell and elongate, and led to failure of complete normal division. This is probably due to inactivation of a cell constituent necessary for subdivision which becomes bound to penicillin. The substance is probably gradually reformed after exposure to penicillin. Secondly, the staining reaction of affected organisms alters, and this is taken as evidence of deterioration in their metabolism. Pratt quotes Gale and others, who found that staphylococci exposed to penicillin could not absorb glutamic acid from their environment. These observers concluded that sensitivity to penicillin was actually confined to those organisms which relied upon their environment for glutamic acid, in contrast to those which were capable of synthesizing it. They also observed that bacteria not only lost their capacity to absorb substances necessary for their metabolism, but also became unable to retain bodies already dissolved within them—for example, lipides and their fatty acid hydrolysates, nucleotides *et cetera*, leak out of affected bacteria.

Pratt stated that their experiments suggested that the over-all effect of penicillin on sensitive bacteria might be traceable ultimately to excessive dehydrogenation of reduced substances, causing alteration of energy relationship of the bacteria so that they could no longer absorb nutriment from outside or retain their cellular constituents. "Terramycin" caused similar reactions. These reactions were interpreted as being specific and not associated with death, because they were so different from those caused by streptomycin, aureomycin or chloramphenicol.

Smith detailed extensive investigations of the effects of "Chloromycetin". The enormous complexity of this work was revealed by the number of metabolic processes and enzymatic systems which came under scrutiny. One is apt to forget that a small organism, such as a bacterium, has complicated metabolic properties similar qualitatively to those of its host. The processes of respiration, carbohydrate utilization, protein and amino-acid utilization, fat and ester utilization and organic acid utilization are all referred to, as well as numerous enzymatic processes. Smith concluded that "Chloromycetin" inhibited more than one enzymatic process in a single organism. Similar extensive investigations of the mode of action of aureomycin, "Terramycin", "Chloromycetin" and streptomycin have been carried out. All these substances interfere with essential metabolic processes within bacteria. It was pointed out that penicillin and streptomycin were synergistic occasionally, but never antagonistic. Similarly, "Terramycin", aureomycin and "Chloromycetin" might assist but not oppose each other. As a group, however, they might be antagonistic to streptomycin and penicillin, but the reverse could not be demonstrated.

Finally, I should like to refer to the work of Mackness upon streptomycin and "Terramycin" with regard to intracellular bacteriostasis. Tubercle bacilli within cells are more vulnerable to "Terramycin" than streptomycin, in that a weak concentration of the former (on a weight-volume basis) is necessary for activity. It is suggested that the cell membrane may have selective screening activities against antibiotics.

I have mentioned these studies in order to emphasize one far-reaching avenue of knowledge that is gradually being traversed as a result of antibiotic therapy. To refer

to antibiotics as being bacteriostatic is to state an effect of their action, but not to give the method of action. Bacteriologists and allied scientists have been provoked to find out why these therapeutic substances destroy bacteria but not the hosts of the bacteria. In the course of this study the respiration, nutrition and metabolism of bacteria have been intensively investigated. Although the conclusions reached are few and perhaps tentative, one feels we are on the threshold of immense discoveries in the biochemistry and biophysics of these minute organisms.

Much has been said about the abuse of antibiotics. At the risk of being tedious I wish to make brief reference to the subject. Norman Lake (1952) states: "To listen to some of our recently qualified doctors one would get the impression that no one recovered from infectious illnesses before the introduction of the new medicaments." He protests against the unthinking universal employment of antibiotics. The editor of the *British Medical Journal* makes comment on this letter. The abuse of antibiotics presented us with surgical as well as medical problems. In lung surgery, bone surgery and dental surgery, and in surgery upon widely infected tissues, the so-called antibiotic cover is indicated, because operation in these fields is known to carry the danger of acute dissemination of bacteria and metastatic infection. However, my surgical colleagues consider it wise in many so-called "clean" operations to have a penicillin or similar "cover". Here is involved the risk of hardening any bacteria present against penicillin, so that if the "cover" actually fails to prevent infection, such infection may well be found to be penicillin-resistant. Further, this widespread use of penicillin *et cetera* will result in extensive penicillin resistance amongst the common pathogenic organisms. Finally, as the editor of the *British Medical Journal* has pointed out, it is apt to increase penicillin sensitivity amongst human beings—a condition which the editor thought was increasing in medicine. However, the surgeon knows what he is doing. He elects to protect his patient temporarily—for the time of his operation and after-treatment—against those organisms which he considers likely to cause infection. He chooses the appropriate antibiotic, whether it is penicillin in general surgery or streptomycin in the surgical treatment of tuberculosis. The same cannot be said of many physicians who firstly treat trivial complaints with an armament of antibiotics, and secondly fail to institute bacterial examinations and sensitivity tests in conditions like pneumonia, bronchitis, pyelitis *et cetera*, but treat by guesswork. A great responsibility rests upon the medical profession to use these great drugs wisely.

The antibiotics save young lives as well as old. They lessen the complications of acute infections—for example, bronchiectasis. They cure or mitigate chronic diseases like syphilis, which in their late manifestation turn the middle-aged into old men and bring them to a premature death.

One cannot yet measure the period by which these agents will prolong life. I know quite well that improved hygiene, nutrition and public health measures are working in this same direction, particularly in the early years of life. However, the new drugs are having a greater effect than any other measure or combination of measures upon prolonging life. They are likely to change the whole pattern of our social structure. They will force on us the problem of reorientating ourselves to these changed conditions.

#### Conclusion.

A Chinese philosopher, when urged by an importunate friend to hurry for a train and thereby save twenty minutes, asked his friend: "What do you propose to do with the twenty minutes you save?" We might ask ourselves what we propose to do with the lives we have lengthened and with the society we have changed. Perhaps if he were here, Bancroft could have supplied valuable help. And thus we return to our distinguished predecessor.

It is difficult to project one's mind into that of another individual, especially one of a former generation. One thing is certain: if Bancroft were alive today he would be more than proud of this great city, of the university

and the medical school. He would take pride in the high standard of professional skill to be found in Queensland. Furthermore, I believe he would be modestly thankful that his successors should hold him and his work in such high esteem.

Long may his memory live. May generations of doctors continue to contemplate his full life and derive inspiration from the study of his work and methods.

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### THE EFFECT OF "DIAMOX" ON OEDEMA IN CONGESTIVE HEART FAILURE.

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WITH a view to assessing the diuretic action of "Diamox" (2-acetylamine-1,3,4-thiadiazole-5-sulphonamide), five in-patients suffering from congestive cardiac failure were given the drug orally and observed over a period of two months.

"Diamox" is a member of the sulphonamide group which has a marked inhibitory effect on the carbonic anhydrase system. The existence of this enzyme, carbonic anhydrase, which catalyzes the hydration and dehydration of carbon dioxide throughout the body, was proved in 1931 (Brinkman, Margoria, Meldrum and Roughton, 1931). Later its presence in the renal tubules was confirmed (Davenport and Wilhelm, 1941), and it has been postulated that in the renal tubules carbonic anhydrase catalyzes the hydration of carbon dioxide to carbonic acid. From the carbonic acid so formed, hydrogen ions are available which are exchanged for sodium ions of the tubular fluid. The sodium ions are returned to the venous blood as sodium bicarbonate, and the hydrogen ions are excreted in the urine with ammonia and as titratable acid. If the carbonic anhydrase is inhibited, the hydration of carbon dioxide is retarded, less hydrogen ion is available to replace the sodium ion in the tubular fluid, and so more sodium ion remains in the tubules and is excreted in the urine. In 1945 Davenport reported that sulphanilamide inhibited carbonic anhydrase. Acidosis had been reported as resulting from sulphonamide administration (Southworth, 1937), and later Davenport reported that sulphanilamide inhibited carbonic anhydrase (Davenport, 1945). The sulphonamides were found to be specific inhibitors of carbonic anhydrase. They do not affect other enzymes. Later diuresis was reported in congestive

heart failure following the administration of sulphonamide (Schwartz, 1949). By 1950 a heterocyclic sulphonamide, "Diamox", had been developed, which has high activity against carbonic anhydrase (it is about 64 times as potent as sulphanilamide) and minimal chemotherapeutic action. It has the additional advantage of being effective when given by the oral route, and it has low toxicity. It is rapidly absorbed unchanged into the blood-stream, and its excretion rate allows a therapeutic level to persist for eight to twelve hours without any cumulative effect.

Its diuretic effect with sodium depletion in man has been reported in normal persons and in those with congestive heart failure (Friedberg, Halpern and Laymor, 1952). As potassium ion competes in the tubules with sodium ion and hydrogen ion, the use of "Diamox" leads to increase in

TABLE I.

Subject.	Age. (Years.)	Clinical Condition.
A. . . . .	53	Congestive cardiac failure from pulmonary heart disease.
B. . . . .	65	Congestive cardiac failure from hypertensive heart disease.
C. . . . .	50	Congestive cardiac failure from coronary atherosclerosis.
D. . . . .	72	Congestive cardiac failure from coronary atherosclerosis.
E. . . . .	70	Congestive cardiac failure from hypertensive heart disease, with prostatic nephropylitis.

potassium output also. At the same time reduction in blood bicarbonate content and increase in blood acidity occur, with a tendency to general acidosis. Therefore further investigation is necessary to ascertain if the drug can be given in clinical practice without producing serious hypokalemia and acidosis. The purpose of this study was an attempt to evaluate how effective a diuretic it was compared with the mercurial diuretics, and if it could be used in clinical practice without undue risk. As the obtaining of a sufficient number of cases for an adequate statistical evaluation was not practicable, no attempt is made to present this work as a statistical study. The conclusions arrived at are essentially clinical impressions of the reactions of five patients, compared with the clinical experience with many similar patients treated during the past ten years with bed rest, digitalis and mercurial diuretics.

The subjects for the clinical trial were indoor patients (all men), selected as they were admitted to hospital, the criterion for selection being the presence of congestive cardiac failure. The main clinical features of the five patients are summarized in Table I.

All patients were treated with complete bed rest, a diet of low salt content (to two grammes of sodium daily) and digitalis. Mercurial or other diuretics were not given. The patients' clinical state was evaluated and listed, as well as their electrocardiograms, chest X-ray films, body weight, fluid balance and blood electrolytes. Two days

TABLE II.  
Data Concerning J.W., Male, Aged Sixty-five Years.

Date.	Days.	Intake. (Mils.)	Output. (Mils.)	Serum Chloride. (Milligrammes per Centum.)	Serum Sodium. (Milligrammes per Centum.)	Serum Potassium. (Milligrammes per Centum.)	Carbon Dioxide Combining Power. (Volumes per Centum.)	Clinical State.
July 7, 1953 . .	0	1440	1670	573	323	20.6	62	Orthopnoea. Crepitations. Ankle oedema.
July 8, 1953 . .	1	1350	1900	—	—	—	—	No orthopnoea. No crepitations. No oedema.
July 9, 1953 . .	2	1420	2070	—	—	—	—	Clear.
July 10, 1953 . .	3	1800	2800	593	315	23.1	70	Clear.
July 11, 1953 . .	4	1470	—	—	—	—	—	Clear.
July 12, 1953 . .	5	1380	2320	—	—	—	—	Clear.
July 13, 1953 . .	6	1610	2430	593	330	20.1	58	Clear.
July 14, 1953 . .	7	1590	2020	—	—	—	—	Clear.
July 21, 1953 . .	14	—	—	581	330	24.2	66	Clear.

TABLE III.  
Data Concerning V.H., Male, Aged Fifty-three Years. Suffering from Pulmonary Heart Disease.

Date.	Day.	Intake. (Mils.)	Output. (Mils.)	Serum Chloride Content. (Milligrammes per Centum.)	Serum Sodium Content. (Milligrammes per Centum.)	Serum Potassium Content. (Milligrammes per Centum.)	Carbon Dioxide Combining Power. (Volumes per Centum.)	Clinical State.
June 29, 1953 ..	—	—	—	510	330	13.6	88	Cyanosis ++. Dyspnoea ++. Rales ++.
July 2, 1953 ..	0	1590	1380	—	—	—	—	Rales ++.
July 3, 1953 ..	1	1770	2690	533	330	16.6	62	Cyanosis +. No dyspnoea.
July 4, 1953 ..	2	1680	2530	—	—	—	—	Rales +.
July 5, 1953 ..	3	1670	2770	—	—	—	—	Cyanosis +. No rales.
July 6, 1953 ..	4	1890	2560	—	—	—	—	No dyspnoea.
July 7, 1953 ..	5	1960	2800	—	—	—	—	Clear.
July 8, 1953 ..	6	1530	3100	—	—	—	—	Clear.
July 9, 1953 ..	7	1450	2200	—	—	—	—	Clear.

TABLE IV.  
Data Concerning E.O.F., Male, Aged Fifty-nine Years. Suffering from Hypertensive Cardiac Failure.

Date.	Days.	Body Weight. (Stone, Pounds.)	Intake. (Mils.)	Urine Volume. (Mils.)	Serum Chloride Content. (Milli- grammes per Centum.)	Serum Sodium Content. (Milli- grammes per Centum.)	Serum Potassium Content. (Milli- grammes per Centum.)	Carbon Dioxide Combining Power. (Volumes per Centum.)	Clinical (Edema).
July 25, 1953 ..	0	11 5 4	1530	5470	533	325	24.0	70	Pitting oedema up to both knees.
July 26, 1953 ..	1	10 8 0	1470	7000	—	—	—	—	No clinical oedema.
July 27, 1953 ..	2	9 12 0	1800	3970	—	—	—	—	No oedema.
July 28, 1953 ..	3	9 9 8	1500	2270	—	—	—	—	No oedema.
July 29, 1953 ..	4	9 8 8	1710	1850	569	300	23.5	52	No oedema.
July 30, 1953 ..	5	9 9 4	1440	2010	—	—	—	—	No oedema.
July 31, 1953 ..	6	9 10 4	1680	1190	—	—	—	—	No oedema.
August 1, 1953 ..	7	9 8 1	1540	3520	—	—	—	—	Few rales left lung base.
August 2, 1953 ..	8	9 6 7	1640	2620	—	—	—	—	No clinical oedema.
August 3, 1953 ..	9	9 5 4	Not recorded	—	533	300	24.7	55	No oedema.

TABLE V.  
Data Concerning J.K., Male, Aged Seventy-two Years.

Date.	Days.	Body Weight. (Stone, Pounds.)	Intake. (Mils.)	Urine Volume. (Mils.)	Serum Chloride Content. (Milli- grammes per Centum.)	Serum Sodium Content. (Milli- grammes per Centum.)	Serum Potassium Content. (Milli- grammes per Centum.)	Carbon Dioxide Combining Power. (Volumes per Centum.)	Clinical (Edema).
August 19, 1953	1	11 9½	1440	1020	541	310	18.5	63	Pitting oedema of both ankles six inches above joint.
August 20, 1953	2	11 9	1550	1250	565	310	18.2	57	Edema less marked—still six inches above ankle.
August 21, 1953	3	11 9	1500	1380	—	—	—	—	No ankle oedema— crepitant rales, both bases.
August 22, 1953	4	11 10	1610	960	577	315	17.7	68	Rales both bases.
August 23, 1953	5	11 12	1620	960	—	—	—	—	Fine rales both bases.
August 24, 1953	6	11 10	1560	1230	589	315	15.5	53	Right base clear. Left base fine crepitant rales.
August 25, 1953	7	11 10½	1500	960	601	315	17.6	47	NIL
August 26, 1953	8	11 13	1130	1420	—	—	—	—	NIL
August 27, 1953	9	11 10½	1610	1840	577	310	17.2	54	Very slight pitting oedema ankles.
August 28, 1953	10	—	1410	1290	—	—	—	—	NIL
August 29, 1953	11	—	—	—	—	—	—	—	NIL
August 30, 1953	12	—	—	—	—	—	—	—	NIL
August 31, 1953	13	—	—	—	589	315	19.9	52	NIL.

after admission to hospital they were given "Diamox" in 0.25 gramme tablets by mouth twice daily, morning and evening, and tablets of digoxin, 0.25 milligramme three times daily. Their clinical state, fluid balance and weight were assessed each day, and their blood electrolytes were estimated periodically. Their individual responses are listed in Tables II to VI.

#### Discussion.

In each case diuresis occurred within forty-eight hours of taking "Diamox" by mouth. In two cases the diuresis was well established within twenty-four hours and all clinical oedema had disappeared within forty-eight hours. Neither of these cases (the patients were B. and C.) was a gross case of congestive failure, but they were of

TABLE VI.  
Data Concerning H.W., Male, Aged Seventy Years.

Date.	Days.	Body Weight. (Stone, Pounds.)	Intake. (Mils.)	Urine Volume. (Mils.)	Serum Chloride Content. (Milligrammes per Centum.)	Serum Sodium Content. (Milligrammes per Centum.)	Serum Potassium Content. (Milligrammes per Centum.)	Carbon Dioxide Combining Power. (Volumes per Centum.)	Clinical (Edema.
September 16, 1953	1	11 2	1320	2100	589	322	19.0	58	Pitting oedema of both thighs and sacrum.
September 17, 1953	2	11 1½	—	—	—	—	—	—	As above.
September 18, 1953	3	11 1½	1350	2610	637	315	18.4	62	As above.
September 19, 1953	4	10 12	1110	3330	—	—	—	—	As above.
September 20, 1953	5	10 6	1410	3720	—	—	—	—	No change.
September 21, 1953	6	10 5½	800	2760	541	310	17.2	56	Still pitting oedema of both thighs, but less marked.
September 22, 1953	7	10 3½	990	4160	—	—	—	—	As above.
September 23, 1953	8	9 10½	1350	2000	613	310	19.5	59	Oedema up to right knee and halfway up left leg.
September 24, 1953	9	9 9	1170	2360	—	—	—	—	No oedema of legs—still sacral oedema.
September 25, 1953	10	9 7	960	670	—	—	—	—	Sacral oedema.
September 26, 1953	11	9 5½	990	960	—	—	—	—	Sacral oedema.
September 27, 1953	12	—	1140	920	613	330	19.0	51	Sacral oedema.
September 28, 1953	13	9 3½	1350	4120	—	—	—	—	Sacral oedema.
September 29, 1953	14	8 13	1260	3460	—	—	—	—	Sacral oedema.
September 30, 1953	15	8 10½	1440	2370	—	—	—	—	No oedema.
October 1, 1953 ..	16	—	1320	2400	577	330	18.5	43	No oedema.

more than moderate severity. Whereas the patients had pitting oedema to the knees at the onset of treatment, all clinical oedema was gone within forty-eight hours, and the oedema has not returned in the following three months. In two other cases the oedema had been dissipated within a week, and in the remaining case by the fifteenth day. The impression gained was that "Diamox" was just as effective as the mercurial diuretics in controlling oedema, perhaps more effective. There was no gross disturbance of the blood electrolytes. Values for serum chlorides, serum sodium and serum potassium were always within normal limits. The carbon dioxide combining power (alkali reserve) was hardly affected. Patient E. developed gross prostatic retention of urine a week after the suspension of "Diamox" therapy. Renal infection and renal failure followed. He died three days later, probably of renal failure. His blood urea content rose to 310 milligrammes per centum. Three patients have continued to take "Diamox" daily for three months after discharge from hospital under out-patient supervision. Of these, one (B.) is symptom-free and clinically well, and has returned to work as a night watchman. The other two have not had a recurrence of oedema, but have dyspnoea on exertion.

The risk of acidosis from depression of alkali reserve does not appear to be great. Suspension of administration of the drug results in the restoration of carbonic anhydrase in twelve hours, with rapid restoration of the alkali reserve.

#### Summary.

From this study of "Diamox" in five cases of congestive cardiac failure the impressions were gained (i) that "Diamox" taken orally is a powerful diuretic, (ii) that it is reasonably free of toxicity and can be taken continuously for five months, and (iii) that it is effective when given by the oral route.

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#### HYPERTENSION: A SURVEY OF AUTOPSY FINDINGS FROM PATIENTS OVER AND UNDER THE AGE OF FORTY YEARS.

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HYPERTENSION with its associated conditions and sequelae is probably the greatest medical problem which the white races have to face. For example, in the period between July, 1950, and August, 1953, 1083 patients came to autopsy from the public wards of the Royal Prince Alfred Hospital, of whom 299 for certain bore the stigmata of hypertension, 200 actually having died because of this or associated conditions. That is, 18.5% of all autopsies in that period were brought about by hypertension, its associated conditions or sequelae.

A statistical analysis of these autopsies has been carried out, and is the subject of this paper. The criteria of hypertension used were as follows: (i) a constant systolic pressure of 150 millimetres of mercury or more; (ii) a constant diastolic pressure of 100 millimetres of mercury or more.

In some cases the blood pressure in the terminal illness was below the levels just given, and in these a definite history of hypertension from the recommending medical officer or indubitable post-mortem evidence was needed for them to be included. The autopsy evidence needed was cardiac hypertrophy of a considerable extent—that is, a heart weight of over 400 grammes when the increase was due to left ventricular hypertrophy with no obvious cause such as a valvular lesion—together with hypertensive nephrosclerosis. Consequently several subjects who could well have been hypertensive to a greater or lesser degree have been excluded from this series.

In Table I are shown the conditions found at autopsy which we consider to be responsible for the hypertension. Thus we found that 21.3% of patients aged forty years and more had a demonstrable cause for their raised blood pressure, compared with 40.9% aged under forty years. The number in the latter group was small, so a further survey was carried out back to January 1, 1940, from which 79 more cases were collected, to bring the total of the subjects aged under forty years to 101. In this larger group 47.5% had a demonstrable cause for their hypertension.

Naturally the great proportion of these demonstrable causes were of renal origin; of the group aged forty years and over, in 20.6% the hypertension had its origin in renal disease, compared with 38.6% in the younger group. With regard to the individual kidney disorders, chronic

TABLE I.  
July, 1950, to August, 1953.

Causes or Type of Hypertension.	Subjects Aged Over 40 Years.		Subjects Aged Under 40 Years.	
	Number.	Progressive Total.	Number.	Progressive Total.
<b>Renal causes:</b>				
Chronic pyelonephritis ..	33	—	1	—
Chronic glomerulonephritis ..	16	—	5	—
Congenital renal anomalies ..	7	—	—	—
Diabetic glomerulosclerosis ..	1	—	—	—
	57	57 (20.6%)	6	6 (27.3%)
<b>Polyarteritis nodosa</b> ..	1	—	—	—
<b>Polycythemia</b> ..	—	—	1	—
<b>Phaeochromocytoma</b> ..	—	—	2	—
<b>Coarctation of aorta</b> ..	—	—	—	—
<b>Thyrotoxicosis</b> ..	1	—	—	—
	2	59 (21.3%)	3	9 (40.9%)
<b>Essential hypertension</b> ..	218 <sup>1</sup>	—	13 <sup>2</sup>	—
<b>Total</b> ..	277	—	22	—

<sup>1</sup> 78.7% of 277.

<sup>2</sup> 59.1% of 22.

glomerulonephritis and chronic pyelonephritis were, of course, by far the most common, and over the same period of time (July, 1950, to August, 1953) there were 34 cases

TABLE II.  
Hypertension in Subjects Aged Under Forty Years, from 1940 to 1953.

Causes or Type of Hypertension.	Number of Subjects.	Progressive Total.
<b>Renal causes:</b>		
Chronic glomerulonephritis ..	30	—
Chronic pyelonephritis ..	5	—
Polycystic kidneys ..	1	—
Aberrant renal artery ..	1	—
Calculus pyonephrosis ..	1	—
Tuberculous pyonephrosis ..	1	—
	39	39 (38.6%)
<b>Coarctation of the aorta</b> ..	3	—
<b>Phaeochromocytoma</b> ..	2	—
<b>Polycythemia vera</b> ..	2	—
<b>Thyrotoxicosis</b> ..	1	—
<b>Plumbism</b> ..	1	—
	9	48 (47.6%)
<b>Essential hypertension</b> ..	53 <sup>1</sup>	—
<b>Total</b> ..	101	—

<sup>1</sup> 52.5% of 101.

of chronic pyelonephritis compared with 21 cases of chronic glomerulonephritis. However, it is interesting to note their numbers in each of the complete groups; thus in the older group there were 33 cases of the former compared with 16 cases of the latter, whereas in those aged under

forty years there were 30 cases of chronic glomerulonephritis to only five of chronic pyelonephritis. That is, chronic glomerulonephritis accounted for 29.7% of the hypertensive patients aged under forty years, and was responsible for 77% of the renal causes of hypertension. This figure came as rather a surprise to us, for we had formed the impression from the literature, and from the clinical teachings in this hospital, that chronic pyelonephritis together with other types of renal disease was at least as common as, if not more common than, chronic glomerulonephritis.

Turning now to essential hypertension, we found that this was the commonest cause in each group—218 of 277 (78.7%) in the older group, and 53 of 101 (52.5%) in those aged under forty years. The figures for the younger group do not agree with those published by Platt (1948), in which, of 64 hypertensive patients aged under forty years, only 16 were diagnosed as having essential hypertension. In this regard it should be remembered that

TABLE III.  
Principal Causes of Death in Essential Hypertension.

Cause of Death.	Subjects Aged 40 Years and Over.	Subjects Aged Under 40 Years.
Intracranial hemorrhage ..	20.7%	30.2%
Cardiac failure ..	13.3%	3.8%
Myocardial infarction ..	13.3%	3.8%
Renal failure ..	7.3%	13.2%
Cerebral infarction ..	4.5%	—
Intercurrent diseases ..	38.0%	43.4%

Platt's figures come from a clinic which is specially interested in hypertension and renal disease, whereas those in this paper are simply the results found in a general hospital. Thus 23 of the 53 patients with essential hypertension in this series died from causes not related to the hypertension, and the great majority of these were only moderately hypertensive (say 180 millimetres of mercury,

TABLE IV.  
Mode of Death in Malignant Hypertension.

Mode of Death.	Number of Subjects.
Renal failure ..	14 (70.0%)
Intracranial hemorrhage ..	4 (20.0%)
Congestive cardiac failure ..	1
Intercurrent disease ..	1

systolic pressure, and 100 millimetres, diastolic), so that but for the intercurrent disease the hypertension probably would not have been discovered for some years at any rate.

#### Hypertensive Effects Causing Death.

With regard to the hypertensive effects causing death, we found that in the older group 181 subjects (65.3%) died as a result of either the hypertension with its associated conditions or the disease producing the hypertension. In those aged under forty years, the figure is 75.2%—that is, 76 of 101 patients.

It should be noted that the cause of death has been listed as a single factor in each case; when more than one condition appeared to be playing a part we have chosen the one that from the clinical notes and autopsy findings seemed the most important. Table III shows the findings in essential hypertension itself, and the results of the individual diseases are shown in the complete figures for both groups given in Tables V and VI.

TABLE V.  
Analysis of Findings in Subjects Aged Forty Years and Over.

Clinical Condition and Number of Subjects.	Condition Found at Post-Mortem Examination.									Deaths Related to Increased Blood Pressure.
	Intracranial Hemorrhage.	Congestive Cardiac Failure.	Myocardial Infarction.	Renal Failure.	Cerebral Infarct.	Dissecting Aneurysm.	Hypertensive Encephalopathy.	Ruptured Aortic Aneurysm.	Ruptured Aortic Cusp.	
Essential hypertension (218) ..	45	29	29	16	10	3	1	1	1	185
Chronic pyelonephritis (33) ..	6	7	3	6	2	—	—	—	—	24
Chronic glomerulonephritis (16) ..	1	1	—	10	1	—	—	—	—	13
Hydronephrosis (congenital) (2) ..	—	1	—	1	—	—	—	—	—	2
Polycystic kidney (1) ..	—	—	—	1	—	—	—	—	—	1
Diabetic glomerulosclerosis (1) ..	—	—	—	1	—	—	—	—	—	1
Polycystic kidney (2) ..	—	1	—	—	—	—	1	—	—	2
Agonistic kidney (1) ..	—	1	—	—	—	—	—	—	—	1
Absent renal artery (2) ..	—	—	—	1	—	—	—	—	—	1
Thyroiditis (1) ..	—	1	—	—	—	—	—	—	—	1
Total (277) ..	52	41	32	36	13	3	2	1	1	181

TABLE VI.  
Analysis of Findings in Subjects Aged Under Forty Years.

Clinical Condition and Number of Subjects.	Condition Found at Post-Mortem Examination.								Deaths Related to Increased Blood Pressure.
	Intracranial Hemorrhage.	Renal Failure.	Congestive Cardiac Failure.	Myocardial Infarction.	Cerebral Infarct.	Hypertensive Encephalopathy.	Lead Encephalopathy.	Dissecting Aneurysm.	
Essential hypertension (53) ..	16	7	2	2	1	1	—	1	30
Chronic glomerulonephritis (30) ..	—	25	5	—	—	—	—	—	30
Chronic pyelonephritis (5) ..	—	3	1	—	—	—	—	—	4
Polycystic kidney (1) ..	1	—	—	—	—	—	—	—	1
Absent renal artery (1) ..	—	—	—	—	—	—	—	—	—
Calculus pyelonephrosis (1) ..	—	1	—	—	—	—	—	—	1
Tuberculous pyelonephrosis (1) ..	—	1	—	—	—	—	—	—	1
Coarctation (3) ..	2	—	1	—	—	—	—	—	3
Phaeochromocytoma (2) ..	—	—	2	—	—	—	—	—	2
Polycythemia vera (2) ..	—	—	1	1	—	—	—	—	2
Thyroiditis (1) ..	—	—	1	—	—	—	—	—	1
Plumbism (1) ..	—	—	—	—	—	—	1	—	1
Total (101) ..	19	37	13	3	1	1	1	1	76

### Malignant Hypertension.

The criteria used for malignant hypertension include the presence of acute renal failure, the anatomical change of thrombocytosis of arterioles, and proliferative glomerulonephritis in addition to the criteria employed for benign hypertension. These criteria were rigidly applied, and some cases on the borderline were discarded. It is interesting to note that the only cases fulfilling these requirements were all primary—that is, there was no demonstrable antecedent cause for the hypertension. In both the series there were 20 cases altogether, 12 (5.5%) occurring in the older group (218) and eight (15.1%) in the younger group (53). These figures would appear to suggest that malignant hypertension is relatively more common in the younger age group, although the numbers are too small to allow definite conclusions to be drawn.

Table IV shows the causes of death found in the subjects of malignant hypertension.

### Conclusion.

In conclusion, we should like to stress that we are not attempting to belittle the importance of primary renal disease in hypertension. From the point of view of prognosis and possible treatment it is imperative to do one's utmost to determine whether there is such an underlying cause. However, we believe that in relation to younger people, at any rate, the pendulum has swung too far, and our figures appear to support the view that essential hypertension is still the commonest cause of raised blood pressure in persons aged under forty years.

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# STILBCESTROL INHIBITION OF ADRENAL CORTICAL TRANSPLANT. REGENERATION.

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THE successful auto-transplantation of adrenal glands into various sites of the body in experimental animals has been described frequently and there is a review of this subject by Grollman (1936). It was early recognized that the medulla degenerated and became necrotic when the whole gland was transplanted, and there emerged subsequently the fact that the capsule, or a part thereof, was capable on auto-transplantation of reproducing practically the identical adrenal cortical pattern that existed originally. The particular factors involved in this controlled phenomenon have not been clearly defined, although pituitary trophic factors are obviously involved.

In the course of preparation of animals for another experiment, the capsules of adrenal glands in one group of rats had been auto-transplanted into the spleen. Sixteen days after this operative procedure, and after salt had been withdrawn from drinking water, stilbcestral pellets were implanted subcutaneously. In this group, all animals died within eight days. Comparable groups without stilbcestral implants survived and remained healthy. From past experience with adrenal transplants, it appeared that stilbcestral exerted a retrogressive influence on the transplants. The present experiment was designed to determine the effect of stilbcestral on adrenal transplant regeneration and to try to gain some insight into the particular pituitary factors inhibited by this simultaneous administration of a synthetic oestrogen.

## Methods and Material.

Mature female albino rats of the Wistar strain weighing between 125 and 155 grammes were used for the main part of the experiment. For the growth hormone test using "plateaued" animals (Marx, Simpson and Evans, 1942), female rats between 200 and 220 grammes and six to eight months old were used. Adrenal auto-transplants into the spleen were performed by a method previously described (Read, 1951). W. K. Whitten (personal communication) suggested the implantation of adrenal cortical tissue under the capsule of the kidney. Hypophysectomies were carried out by a modification of the original classical procedure (Smith, 1930). Stilbcestral was implanted subcutaneously in eight-milligramme pellets and ACTH<sup>2</sup> was injected subcutaneously in two-milligramme doses per rat per day for two weeks. The animals were fed our stock diet with 1% saline in the drinking water of the adrenal transplant groups and sucrose, in addition, for the hypophysectomized rats. At the completion of the experiment, after fourteen days, surviving animals were sacrificed and the adrenal transplants carefully dissected from surrounding tissue after being fixed in Bouin's solution. The dry adrenals were weighed on a torsion balance.

## Results.

1. When normal "plateaued" female rats were used in groups of eight experimental animals and eight controls, there was no evidence of growth hormone in the ACTH used over a fifteen-day injection period.

2. The design and results of the experiment on the effect of stilbcestral on adrenal auto-transplants are set out in Table I.

## Discussion.

The presence of growth hormone in the commercial preparation of ACTH was not detected by the one test used. There may be two interpretations of this—either

growth hormone was present and was inhibited by ACTH (Marx, Simpson, Li and Evans, 1943; Smith, Sayers, Gosh and Woodbury, 1952) or alternatively, growth hormone was absent. No collateral experiments were carried out in the present series in an attempt to determine this issue. The interference of ACTH with growth, gonadotropic and thyrotropic hormones can be overcome by using adrenalectomized and hypophysectomized assay animals (Smith *et alii*, 1952), but this assay procedure has not been adopted here. However, the fact remains that there was inhibition of pituitary function by stilbcestral from the point of view of adrenal auto-transplant regeneration.

TABLE I.

The Effect of Diethylstilbcestral Implantation on Survival and Adrenal Regeneration.<sup>1</sup>

Group.	Number of Rats.	Experimental Preparation of Animals.	Number of Animals Dead at End of 14 Days.	Average Time of Survival (Days.)	Average Weight of Adrenal Transplants at Death. (Milligrammes per 100 Grammes.)
A	8	Adrenal auto-transplant to the spleen	—	14	3.3
B	7	Adrenal auto-transplant to the spleen plus stilbcestral	7	9	1.7
C	9	Hypophysectomy plus ACTH	—	14	—
D	9	Hypophysectomy plus adrenal auto-transplant to the spleen plus ACTH	—	14	2.7
E	6	Hypophysectomy plus adrenal auto-transplant to the spleen plus ACTH plus stilbcestral	6	7	1.7
F	7	Adrenal auto-transplant to the kidney	—	14	Not weighed.
G	8	Adrenal auto-transplant to the kidney plus stilbcestral	9	9	Not weighed.

<sup>1</sup> Fourteen days' survival indicates that the rats were sacrificed after fourteen days.

The determination of ACTH activity and its correlation with other biological functions have not been altogether assessed. The measures of ACTH activity have been adrenal weight maintenance (Simpson, Evans and Li, 1943) and ascorbic acid depletion (Sayers, Sayers and Woodbury, 1948). Recently, doubt has been raised regarding the definitive nature of these tests as a comprehensive measure of the same type of ACTH activity, and separate pituitary fractions have been postulated. Mayer, Scheer, Ritter, Tesar, Logan, Oleson and Cox (1952) found that ACTH, after acid hydrolysis, lost considerable activity when measured by the adrenal weight maintenance method, but there was little or no loss when measured by the ascorbic acid depletion test. Ingle and Li (1952) have also found a lack of correlation between ACTH protein and ACTH peptide using various test methods. Young (1951) has suggested two separate substances possessing adrenocorticotrophic activity. In addition, Stack-Dunne and Young (1951) felt that the ascorbic acid depletion test and the term ACTH have come to be regarded as synonymous by many clinicians, who regarded the actions of both as being parallel. Parkes (1951) has suggested that pituitary inhibition by other substances may well lead to the use of relatively intact animals in the assay of pituitary fractions.

In the present experiment, splenic auto-transplantation of adrenals was chosen because of the ease in detection of the auto-transplant and the relatively simple dissection involved. As there is apparently no inactivation of adrenal

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<sup>2</sup> "Acton" (Fredericksberg Chemical Laboratories, Limited, Copenhagen, Denmark).

cortical hormones by the liver (Read, 1951) there appear to be no objections to this site. Groups B, E and G gave comparable results from the point of view of adrenal auto-transplant regeneration and survival of animals. Although there is some difference in the weights of dried adrenal glands in the groups reported, it is felt that the results become less discordant when the time factor is considered and, also, the fact that the stilbœstrol treated animals lost more weight.

The possibility of the direct passage of adrenal steroids into the liver affecting œstrogen breakdown and producing the results observed appears to be ruled out by the results in group G. Whether or not the regeneration of auto-transplanted adrenal cortex is an index of the possible components of ACTH as measured by the ascorbic acid depletion and the adrenal weight maintenance tests has not been clarified.

#### Summary.

The inhibition by stilbœstrol of adrenal gland regeneration after auto-transplantation is described. Comparable results were obtained in rats with adrenal auto-transplants into the spleen and into the kidney, and in rats which had been treated similarly but hypophysectomized and injected with a commercial preparation of ACTH.

#### Acknowledgements.

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### A SPLINT FOR USE DURING BLOOD TRANSFUSION IN INFANTS.

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ON several occasions during the administration of blood transfusions to infants ranging in age from a few days to two years, difficulty has been encountered in properly immobilizing the ankle joint with the methods hitherto used. To facilitate this immobilization a new type of aluminium splint was designed, which is easy to make and very satisfactory if properly applied.

It has several features, as follows: (i) The same splint may be used for either leg. (ii) It is easily adjustable for the size of the infant. (iii) It provides better immobilization of the limb than the gutter type splint. (iv) It provides a rigid fixture for polythene tube connexion.

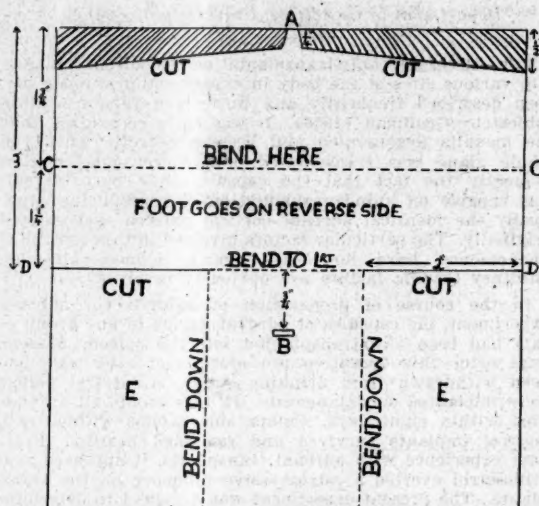


FIGURE I.

#### To Make the Splint.

The measurements shown are for an average size.

Cut a piece of aluminium six inches square, and mark it with pencil as shown in Figure I. On one side cut it away so as to leave a tongue A a quarter of an inch long, which when folded will fit into slot B. C and C' are one

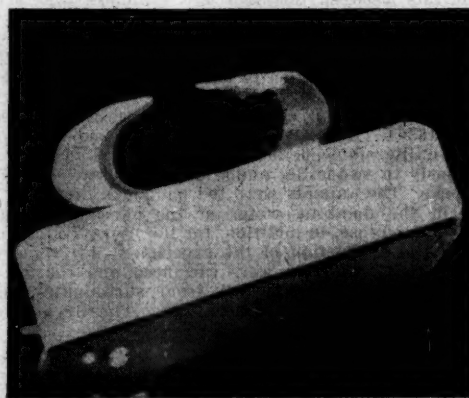


FIGURE II.

and three-quarter inches from the original end, and D and D' three inches from the end. Cut down the line D-D' for two inches on each side. Bend D-D' to a right angle, then C-C' so that A fits into B. E and E' then fold around an ordinary padded wooden splint.

#### To Use the Splint.

The splint is a T-splint and is fixed to the other one by zinc oxide plaster at a distance from one end equal to the length of the infant's leg.

The padded splint is then attached to the four sides of the cot by bandages. Movement of the splint should then be minimal.

Next place the sole of the infant's foot on the flat cross piece by using one or more pieces of zinc oxide plaster from under the cross piece, over the heel and similarly over the dorsum of the foot. A loose bandage fixes the leg to the padded splint.



FIGURE III.

Later the transfusion tube is attached to the top of the cross piece, as shown.

The splint may be covered with zinc oxide plaster for comfort and neatness.

### PHENYLKETONURIA.

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In 1951 a survey at Northfield Mental Hospital revealed that three adult male patients were excreting phenylpyruvic acid in their urine. This phenomenon has been frequently described since its discovery by Föllings in Norway in 1934. Large surveys in the United States of America by Jervis (1939) and by Levy and Perry (1949) have shown that phenylketonuria is limited to the intellectually retarded, 82% of affected subjects being definitely idiots. Phenylketonuric subjects are unable to convert phenylalanine from their diet into tyrosine (mother substance of adrenaline, melanin and other products) and must excrete the ingested phenylalanine as phenylpyruvic acid. In some unknown way this error in metabolism is always accompanied by retardation of cerebral development, though the affected subjects may seem healthy otherwise. An historical review has been given by Cantor (1951) in this journal and need not be repeated here.

This paper suggests new methods of approach, which have been conceived as the outcome of work in Adelaide since 1951. It records observations and investigations

made on the neurological, mental and general physical states of our patients, comparing them with studies made elsewhere, and suggests in addition that the concept of phenylketonuria may be linked to mental illness and mental instability in general, as well as to mental deficiency. It is hoped to make this the subject of a further study; in the meantime a plea is made for an Australian survey, as suggested by Cantor, to provide a significant number of cases for research by any one university.

#### Material of Present Survey.

Specimens of urine of congenitally mentally defective patients were tested by the addition drop by drop of a 5% ferric chloride solution to one inch of urine in a test-tube, acidified with sulphuric acid. Phenylpyruvic acid, if present, produced a deep green colour, sometimes darkening to black, later fading. The test is spectacular and no confusion is possible with the purple-red colour produced by aceto-acetic acid and some drugs, the white precipitate of ferric phosphate, the black of melanic urine, or the deep blue of alcapton urine. Sulphuric acid is used, because a weak acid, such as acetic acid, sometimes gives a false negative result. A confirmatory test with 2:4 dinitrophenylhydrazine was made in each case.

Ninety-six patients were tested at Northfield Mental Hospital (78 males and 18 females), and three phenylketonuric subjects (all males) were found. Of 140 patients tested at Parkside Mental Hospital, no phenylketonuric subjects were found, nor were any found in 200 patients tested at Minda Home, an establishment for the care and education of mentally retarded children. One of the Northfield phenylketonurics had a brother suffering from a severe grade of mental deficiency who had died some years previously at Minda Home. Between them, these three hospitals contain the great majority of severely mentally defective persons in South Australia.

A social worker is studying the families which have produced these phenylketonurics, and her preliminary reports indicate that there may be an immoderate incidence of mental instability, abnormality and psychopathy among the members, such as is sometimes found in the families of other mental defectives.

#### Physical Characteristics.

At a recent clinical meeting in Adelaide addressed by a paediatrician from abroad, it was considered that there was a clinical picture of phenylketonuria, that there were signs by which the diagnosis declared itself, and that a trained worker could pick them out at a glance: a child in regard to whom the diagnosis was in question was instructed to walk, in order to demonstrate whether the "characteristic" spastic phenylketonuric gait was present. This attitude is misleading. Apart from the fair complexion, few features are recorded in the literature as recurring with any degree of constancy in phenylketonuria. Josephy (1948) in Illinois had 16 patients, all of whom were fair haired and had poorly pigmented skin, even when they were of Mediterranean origin and had dark-skinned parents. Of our patients, one has bright red hair with blue eyes, one has sandy hair with blue eyes, and the other has brown hair with brown eyes.

Other features which have been described as typical of phenylketonuria may be related to the mental level. Josephy considers the jerkiness and stooped posture, when they occur, to be so related; similarly related, it seems, may be the rocking movement which has been described, but which in our patients is public masturbation, common in mental defectives; also similarly related may be voluntary repetitive finger movements of a flicking and pill-rolling type. Our patients had normal fundi (confirmed independently by an ophthalmologist); one had epileptic seizures at the rate of one a month; and one had slightly hypertonic lower limbs; otherwise there was no clinical neurological abnormality, except in the autonomic nervous system, as will be described below.

None of our patients had widely spaced incisors or prognathos of maxilla as described by Cowie (1951a).

There was no *pes planus*: in one patient there was partial syndactyly of the second and third toes; in two there was a small gap between the first and second toes. The peripheral circulation seemed normal. One patient had raised blood pressure (190 millimetres of mercury, systolic, and 135 millimetres, diastolic) for which no organic cause could be found; the heart seemed normal (confirmed by a cardiologist).

In only one of our patients was it reasonable to guess at the diagnosis from the clinical signs. Other cases may be more characteristic; but because the condition does not necessarily declare itself, it must be emphasized that the special urine test is obligatory in every case of mental deficiency of every degree, whether other clinical signs are present or not.

#### Mental Status.

Cowie (1951a) carried out quantitative estimations of the output of phenylpyruvic acid of her patients, and found it suggestive that the three patients of highest mentality were amongst those who excreted least phenylpyruvic acid. It is presumed (although the article does not so state) that the diet of Cowie's subjects was controlled, as otherwise a comparison of values would have little point; also for proper significance the daily excretion of phenylpyruvic acid should have been calculated per kilogram of body weight rather than per individual. From this experiment, and from the fact that Cowie's most intelligent subject was the most highly pigmented, it could be conjectured that the metabolic defect can exist in a partial form, with low excretion of phenylpyruvic acid, moderate production of melanin, and some preservation of intelligence. We repeated the experiment with the aid of the Biochemistry Department of the University of Adelaide; the output of phenylpyruvic acid of our patients, estimated as Lovibond units, showed that the patient of highest intelligence excreted least phenylpyruvic acid per kilogram of body weight, and that the patient of lowest intelligence excreted most.

The most intelligent of our patients, X, in addition to excreting the least phenylpyruvic acid, is the most heavily pigmented, having brown hair, a thick skin which tans normally, and brown eyes. He talks readily and is able to do simple work such as "decking" the floor and changing linen of soiled patients. He remained out of mental hospital until the age of thirty years, not with his family, but apparently as the assistant of a travelling hawker of drapery. He has during recent years deteriorated somewhat.

The least intelligent, A, is an idiot who cannot speak, dress or feed himself, but who sits habitually on a bench rocking in the manner of some year-old infants; sometimes his hands engage in rapid stereotyped flicking movements, and he urinates as the whim takes him. He comprehends simple commands such as "stand up", "turn over", but little more.

The mental state of the other patient, Y, is difficult to assess. He gives the impression of being an imbecile, but at the same time he is withdrawn and has the immobility and unapproachability of a catatonic. He keeps his eyes tightly closed and mutters under his breath to himself as though absorbed in autism. He normally exhibits a moderate degree of *flexibilitas cerea*, but at times is impulsive and attacks others without warning. Surmising that his variability indicated that he had regressed to this psychotic condition rather than that his psychic development had been arrested there, Dr. W. Salter and I thought it worthwhile to give him a course of electroconvulsive therapy. No change resulted.

#### Autonomic Nervous System.

If the production of adrenaline was impaired in phenylketonurics, as might be anticipated from the nature of the metabolic error, then the reactivity of the sympathetic nervous system might be expected to be abnormal. Adrenaline, writes Samson Wright, is normally prepared by the adrenal medulla from tyrosine, which is stored in the skin; if the medulla is destroyed, as in Addison's disease, the mother substance is not called upon and accumulates in the skin, where *tyrosinase* converts it into melanin, which is deposited in the Malpighian layer. In phenylketonuria it is postulated that deficiency of the mother substance results in scanty production of melanin,

manifested by fair complexion, and of adrenaline, possibly manifested by a congenital "set" of autonomic reactivity.

The theory was tested by injecting adrenaline intravenously into two of the phenylketonuric patients (the third was not tested because of doubts as to his cardiac condition) and recording the changes in blood pressure and any other responses. Nine "control" patients, of similar mental deficiency to the phenylketonurics, were subjected to the same test.

The patient, at least two and a half hours after a meal, rested in the supine position for at least half an hour, during which time frequent blood pressure readings were taken until the experimenter was satisfied that the systolic blood pressure had fallen to its basal level. Care was taken to have the patient neither hot nor cold, and the test was not performed in extremes of temperature. Tests were not carried out if the patient could not be induced to rest calmly. One cubic centimetre of normal saline was then injected intravenously, and serial systolic blood pressure readings were taken every half minute until the basic level was again reached and maintained. Then 0.025 milligramme of adrenaline in one cubic centimetre of water was rapidly injected intravenously, readings being taken as before until the basal level was again reached and maintained. Any physiological or affective changes in the patient were noted. The readings were plotted on a graph, each tenth inch of the ordinate representing two millimetres of mercury of systolic blood pressure, and each tenth inch of abscissa representing ten seconds of time. Three variables were calculated from the graphs—namely, "rise in blood pressure", "homeostasis time", and "area". "Rise in blood pressure" was the difference in millimetres of mercury between the maximum and the basal systolic blood pressure readings. "Homeostasis time" was the number of seconds elapsing from the injection of adrenaline to the restoration of basal blood pressure. "Area" was the number of square inches enclosed between the curve produced by the blood pressure readings and a line representing the basal blood pressure. The test was performed three times on each phenylketonuric patient, reasonably consistent results being obtained.

The test is similar to the first phase of the test of the reactivity of the autonomic nervous system devised by Funkenstein, Greenblatt and Solomon, of Harvard University (1949).

Results are recorded in Table I, and two characteristic graphs, of a control imbecile and a phenylketonuric imbecile respectively, are shown in Figure 1. Two factors must qualify the validity of the results: firstly, the fact that only two phenylketonurics were available for testing in this series; secondly, the fact that there is a wide variation in response to this injection amongst people of normal intelligence. Nevertheless, the following conclusions are justified: (i) Mental defectives (non-phenylketonuric) have a low sympathetic nervous system reactivity, shown by moderate "rise in blood pressure" (39 millimetres of mercury, average), moderate "homeostasis time" (188 seconds, average), and small "area" (1.93 square inches, average). (ii) The phenylketonuric mental defectives tested reacted more violently to the introduced adrenaline, as was shown by high "rise in blood pressure" (86 millimetres of mercury, average), longer "homeostasis time" (249 seconds, average) and larger "area" (4.59 square inches, average).

In general terms, mental defectives (non-phenylketonuric) exhibit to a low degree the human counterpart of Cannon's fight-flight reaction in cats—that is, they tolerate introduced adrenaline—and presumably their own secretion—with small physiological and affective change. On the other hand, the phenylketonurics tested are sensitive to a high degree to the introduced hormone, which suggests that they may not be familiar with it in their own secretions, or may produce it only too tardily in too small amounts.

Clarification of this assumption must await further work. It is proposed at Northfield to test the response of the phenylketonurics to injected insulin (normally antagonized by adrenaline); theoretically it might be anticipated that

if phenylketonurics produced adrenaline in emergency with difficulty, they should the more easily be rendered comatose by insulin. Direct adrenaline assay of blood in the resting patient by an accurate method, such as that described by Weil-Malherbe and Bone (1952), would also be illuminating.

#### Theory of Mental Defect.

Alvord *et alii* (1950) at Cornell University performed autopsies on five phenylketonurics, and in three cases found defective myelination of parts of the central nervous system. On the other hand, Josephy (1948) found no gross or microscopic changes in his autopsy subjects. Alvord *et alii* suggest that the defective myelination may be produced by the error in phenylalanine metabolism, and may be at least in part responsible for the mental deficiency.

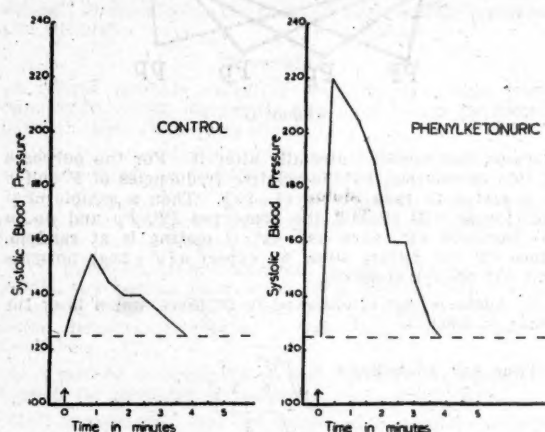


FIGURE 1.

Showing characteristic types of response to rapid intravenous injection of 0.025 milligramme of adrenaline under basal conditions, in a control ament and a phenylketonuric ament.

In the large group of phenylketonurics who seem possessed of structurally normal brains, it is tempting to trace the mental defect to the faulty reactivity of the sympathetic nervous system described above (it being always remembered that the results were obtained from two patients). In a person of normal awareness, a moderate or pronounced response to introduced adrenaline is normal and to be expected. In persons of diminished awareness and decreased ability to respond to stimuli, such as withdrawn schizophrenics or idiots, a weaker response to introduced adrenaline is to be expected, and is in fact obtained. What is unexpected is that the grossly retarded phenylketonurics who were tested reacted vigorously, in the manner of an over-alert, anxious individual of normal intelligence, despite the fact that in their daily life they show little evidence of such responsiveness. This paradox may find its explanation in an abnormality of adrenaline metabolism, related to the known abnormality in phenylalanine-tyrosine-melanin metabolism.

It is not difficult to relate the observed mental defect to abnormality in adrenaline metabolism. It is obvious that if adrenergic activity is abnormal from birth, the learning process is not likely to follow its normal paths. A consideration of the importance of affective processes in learning during early life illustrates this. The housewife spans the puppy to teach it not to urinate on the carpet; the psychotherapist provides conditions under which early learned human behaviour, including fears, guilt, symptoms and rationalizations, can be unlearned. Fundamental factors in the learning process are motivation, stimulus and reward, each frequently possessing a high affective charge. Affective processes are known to be subserved to a large but undetermined extent by the sympathetic nervous system, and to this extent it may prove that the

mental defect of the phenylketonuric is traceable to his apparent abnormality in adrenergic response.

George Moore (1886) summed up the position as follows:

Neither Latin, nor Greek, nor French, nor History nor English composition could I learn, unless, indeed, my curiosity or personal interest was excited—then I made rapid strides in that branch of knowledge to which my attention was directed. A mind hitherto dark seemed suddenly to grow clear, and it remained clear and bright as long as passion was in me; but as soon as passion died the mind began to cloud, and it remained fixed in an almost immovable obtuseness till roused again by the goad of some new impulse.

TABLE I.

Showing Responses of Control and Phenylketonuric Patients to Rapid Intravenous Injection of 0.025 Milligramme of Adrenaline under Basal Conditions.

Subject.	Rise in Blood Pressure. (Millimetres of Mercury.)	Homöostasis Time. (Seconds.)	Graph Area. (Square Inches.)
Controls.			
H. . . . .	25	150	0.89
P. . . . .	30	230	1.61
McC. . . . .	30	150	0.85
B. . . . .	25	180	1.47
B. . . . .	25	120	0.90
B. . . . .	60	180	2.51
B. . . . .	40	240	2.23
M. . . . .	45	230	3.04
O. . . . .	75	210	3.88
Average . .	39	188	1.93
Phenylketonuric Patients.			
X. (1) . . . .	85	240	4.14
(2) . . . .	80	200	4.55
(3) . . . .	70	300	4.21
Y. (1) . . . .	95	270	4.45
(2) . . . .	90	255	5.78
(3) . . . .	95	230	4.38
Average . .	86	249	4.59

Two popular concepts of the relation between the metabolic defect and the mental deficiency have so far stimulated practical therapeutic effort. One is that the accumulation of phenylalanine or one of its derivatives in the tissues of these patients, as shown by Jervis *et alii* (1940), may exert from birth a toxic effect on the brain; the other is that the deficiency of the mother substance tyrosine and its products may impair the function of the brain. The first concept has led to attempts at withdrawing phenylalanine from the diet of the patients, the second to the giving of additional tyrosine to the patients; both experiments have practical difficulties and objections. The experiment adduced above seems to support the second concept.

Related to both concepts is the third, that lack of phenylalanine-tyrosine conversion depends on lack of the necessary enzyme, which is replaced by a less effective or ineffective one. This enzyme may be aberrant in the sort of ways Pauling and others (1949) found characteristic of the abnormal globin of sickle-cell anaemia. Variations in the abnormality of the enzyme protein would determine the greater or lesser amounts of excreted phenylpyruvic acid correlated with more or less severe mental defect. This concept clouds direct therapeutic aspirations: it is scarcely conceivable how sufficient amounts of this enzyme, even could it be isolated, could be introduced into the liver cells of the patients. As a complex protein, its administration would also probably evoke antibodies.

Tredgold, in his text-book "Mental Deficiency", puts forward the concept that the metabolic error is merely an added complication of "ordinary" primary amentia and not the cause of it—analogous to his claim that there is a

distinct class of cretin in whom the essential condition is primary amentia, the hypothyroidism being merely a superadded complication. Tredgold's authority on the subject of phenylketonuria is not enhanced by an unfortunate double reference to "phenylalamine"—unfortunate because his argument that phenylketonurics tend to occur in psychopathic families, just as other aments do, seems valid. In explanation of this, however, Penrose (1935) suggested that the gene for the condition is not completely recessive, but exerts an influence on the heterozygotes ("carriers") predisposing them to mental illness.

#### Problems of Early Diagnosis.

None of the experiments, such as the administration of tyrosine, which so far have been performed on phenylketonurics, have been conducted on a new-born phenylketonuric child. Phenylketonuria is not normally diagnosed until an age when mental defect is apparent, and frequently not even then. If it is ever to be proved or disproved that the condition can be relieved, this work will have to be done on new-born infants before irreversible changes have occurred in the child which make experimentation inconclusive. To take the analogy of cretinism, in which the nature of the metabolic error is accurately known: if administration of the deficient substance, thyroid, is withheld until after the first year, cure is incomplete because permanent damage has already been done, cerebral development, including myelination, having proceeded abnormally. Fortunately for the cretin, his plight is proclaimed at an early age by his appearance, whereas the phenylketonuric is never distinguished and probably resembles the normal infant.

There is only one way to diagnose phenylketonuria at birth, and that is to make a routine urine test of all new-born infants during their stay in the maternity hospital. Such a tedious procedure will be tolerable only if a simple test can be devised which will not be a burden on an already overworked nursing staff. An impregnated filter paper which could be slipped inside the baby's napkin and examined as to colour when the napkin was renewed would provide an acceptable test, provided that the percentage of "false positives" requiring more detailed testing could be kept reasonably low. In Adelaide at present an attempt is being made to devise such a test. Adelaide is not the ideal place for the quest for new-born phenylketonurics, because amongst its small population years may elapse before one is found; however, if in larger centres it was discovered that new-born phenylketonurics could be benefited by biochemical means, the quest would have to become universally a part of maternity hospital procedure. To what extent, if any, the new-born phenylketonuric would have deteriorated *in utero*, or failed of development, would make intriguing table talk for biochemists.

#### Eugenic Considerations.

Phenylketonuria is an inherited disease. It is usually held to be determined by an autosomal recessive gene (although Penrose suggests that heterozygotes tend to be mentally unstable), and for the purposes of eugenic recommendations this simple concept is usually accepted. Recessive genes may be carried on through a stock for generations, and the character which they bear may appear only when, by a proper mating, two recessive genes are brought together in one out of four progeny. If a male having the misfortune to bear the recessive gene for phenylketonuria has the equally rare misfortune to select for his mate a female also having the misfortune to bear the recessive gene, he can produce progeny of which one in four will be phenylketonuric and two in four will be heterozygotes. This may be represented by a diagram (Figure II) in which the gene for phenylketonuria is represented by the symbol *p*, and its normal allele by *P*. The phenotypes of *PP* and *Pp* individuals are normal, that of *pp* individuals is phenylketonuric.

Writers on the backward baby (as Kirman, 1953) are fond of suggesting that the physician's advice on the desirability of having further children, to parents whose

first child is phenylketonuric, should be negative. But if the first child is phenylketonuric each subsequent child still has the three out of four chances that it will not be. Grieving parents should be acquainted with this probability rather than with gratuitous prohibitions.

As a further argument for the undesirability of these parents having more children, it is sometimes observed that two out of four siblings will be heterozygotes—that is, "carriers". But a calculation shows that the frequency of the gene for phenylketonuria in the population is much greater than realized, so much greater that a few "carriers"

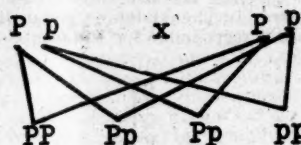


FIGURE II.

more or less cannot materially alter it. For the purposes of this calculation, let the relative frequencies of *P* and *p* be *y* and *x* (*x* then equals  $(1-y)$ ). Then a sample of *n* individuals will contain the genotypes *PP*, *Pp* and *pp* in the numbers  $ny^2$ ,  $2nxy$  and  $nx^2$ , if mating is at random. Since *PP* and *pp* are alike, we expect  $n(y^2 + 2xy)$  normals and  $nx^2$  phenylketonurics.

In Adelaide,  $nx^2$  is observed to be three and *n* is of the order of 400,000.

$$\begin{aligned} \text{Thus, for Adelaide, } x &= \sqrt{\frac{nx^2}{n}} \\ &= \sqrt{\frac{3}{400,000}} \\ &= 0.00274 \end{aligned}$$

This 0.274% represents a gene frequency of one in 365, which means that there is one heterozygous person in about 365/2, or 183. It is estimated in the United Kingdom that the frequency of the disease is about 1:25,000 and a similar estimate is given for the United States of America. This means a gene frequency for these countries of 1:158 and one heterozygous person in about 79. The Adelaide frequency cannot be taken to be significantly less than that in the United Kingdom or the United States of America.

#### Maintenance of Gene in Population.

Such a high gene frequency appears at first sight rather surprising. The phenylketonurics themselves are rare, and in the main genetically lethal—that is, have no progeny—and this infertility represents a loss in each generation. There must be some counteracting influence to keep up the frequency. One possibility is mutation—that is, normal genes turning suddenly to abnormal; the other is slightly greater fertility of heterozygotes. No method is at present available for discriminating between these two possibilities. Values for each of the possibilities have been calculated and will be published later.

If it is assumed that therapy can make phenylketonurics normal, the capacity to reproduce included, it will not make their heredity normal, for they will hand on their defective genes instead of these being lost. Instead of *f* (the reproductive fitness) being zero it will now have a definite positive value. The frequency of the gene in the population will no longer be held in check, but will tend to rise through the occurrence of mutation or the greater fertility of heterozygotes until a new equilibrium is struck, depending on the value of *f* achieved by therapy. The frequency of phenylketonurics thus rises, as does that of the heterozygous carriers. If, as Penrose suggests, these heterozygotes tend to be mentally unstable, the strength of this tendency will be augmented. The worker on the

therapy of phenylketonuria may be experimenting with a Pandora's box comparable with that of atomic science.

#### Biochemical Basis of Mental Instability.

Happily, the successful therapy of phenylketonuria does not seem imminent. But a knowledge of the gene frequency as it exists today suggests one important and completely astonishing consideration. If the calculation that one person in 200 is heterozygous for phenylketonuria is viewed in the light of Penrose's suggestion that these heterozygotes tend to be mentally unstable, the whole subject of mental instability takes on a new biochemical aspect. The possibilities are so alarmingly novel that it is no more than prudent conservatism at this stage to pause before Penrose's suggestion, like Mark Twain's "Innocents Abroad" contemplating the curiosities of Genoa, "harassed with doubts".

#### Summary.

1. Three patients excreting phenylpyruvic acid were found at Northfield Mental Hospital in a survey conducted in South Australian institutions.
2. Clinical observations on these patients are compared with those made on phenylketonuric patients elsewhere.
3. A contrast is made between the responses to adrenaline of two phenylketonuric patients and of nine non-phenylketonuric control aments.
4. A physiological-psychological theory is formulated to explain the mental retardation of phenylketonurics with apparently structurally normal brains—namely, that the mental deficiency is related to abnormality in adrenaline metabolism.
5. A method is suggested of diagnosing phenylketonuria at birth for purposes of research.
6. It is concluded that the danger of successful therapy of phenylketonuria may outweigh its advantages, because a new equilibrium for the gene will be struck, in which a very high proportion of the population will become "carriers" and the disease prevalent.
7. A high gene frequency for phenylketonuria (of the order of one in 200 of the population) is estimated, and it is suggested that this assumes special significance in the light of Penrose's claim that persons known to bear this gene have a tendency toward mental instability.

#### Acknowledgements.

The physical and mental examinations of the phenylketonuric patients were repeated by Dr. W. F. Salter, Deputy Superintendent of Northfield Mental Hospital. Dr. Salter performed several of the adrenaline experiments and took part in discussions. Professor D. G. Catchside, at the Waite Agricultural Research Institute, read the paper and made many helpful suggestions. Dr. T. L. McLarty carried out medical ophthalmoscopic examinations, and Dr. J. M. McPhie examined the cardiovascular system when necessary. Dr. K. N. Steele made available the facilities of Minda Home, Brighton, and urine testing in this establishment was carried out under his aegis. Professor Mark Mitchell, of the Biochemistry Department, University of Adelaide, gave advice and had urinary phenylpyruvic acid estimations carried out. The Superintendent of Mental Institutions in South Australia, Dr. H. M. Birch, approved the performance and publication of the work.

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## Reviews.

**Bodily Changes in Pain, Hunger, Fear and Rage: An Account of Recent Researches into the Function of Emotional Excitement.** By Walter B. Cannon, M.D., S.D., LL.D.; Second Edition; 1953. Boston: Charles T. Branford Company. 8" x 5½", pp. 420, with 43 text figures. Price: \$5.00.

"BODILY CHANGES IN PAIN, HUNGER, FEAR AND RAGE", by Walter B. Cannon, carries a title page marked Second Edition, 1953. It is a reprint of the 1929 edition, which was also the second edition. The suggestion that it is an account of recent researches into the function of emotional excitement is relevant to 1929, not to 1953.

The book is, of course, a classic in physiology, and the manner of setting out the title page is misleading. Anybody wishing to purchase it would do so because it is a classic and not because it contains recent information. This is to be expected because Dr. Cannon died in 1945.

**Human Blood Coagulation: And its Disorders.** By Rosemary Biggs, B.Sc. (London), Ph.D. (Toronto), M.D. (London), and R. G. Macfarlane, M.A. (Oxon.), M.D. (London); 1953. Oxford: Blackwell Scientific Publications. 9" x 6", pp. 424, with three plates and 57 text figures. Price: 32s. 6d.

THE authors of this work lead the British research workers in the field of blood coagulation, and they have now produced the most comprehensive book yet available on the subject. It will prove a valuable physiological monograph, but it was a courageous undertaking on the part of the authors. There is probably no facet of physiology which has advanced so rapidly or become so confused during the past decade, and it has been said with some measure of truth that almost every research worker in the field has eventually proposed a new theory to explain his findings. Biggs and Macfarlane have reviewed with impartiality and authority the position as at the end of 1952 and have added the results of many of their own unpublished observations at the Radcliffe Infirmary, Oxford. Revisions rather than reprints, however, will be necessary at frequent intervals because important contributions have already been made since completion of the work.

The book consists of two parts, the first concerned with physiological aspects and the second with clinical disorders of coagulation. Numerous technical procedures as employed by the authors and other workers are clearly explained in an appendix. The illustrations are mainly line drawings which have the uncommon virtue of simplicity, and the liberal use of textural diagrams facilitates reading. Each of the principal chapters ends with a summary. Usually chapter summaries are not satisfactory either because they are not self-explanatory or because the author uses them to add further remarks. Biggs and Macfarlane have carefully avoided these pitfalls, but their summaries might have been more appropriately placed at the beginning of the chapters.

The book is well produced in the typical style of the publishers. Undoubtedly it will be the standard reference on the subject and therefore will be essential in every physiolo-

logical and pathological laboratory. It will also interest clinicians who desire a lucid and stimulating exposition of a rapidly developing subject with numerous practical applications.

## Notes on Books, Current Journals and New Appliances.

**The Physician's Index of Australia and New Zealand.** Edited by B. G. G. Fegent, M.P.S. (N.S.W.); Third Edition; 1953. Sydney: Butterworth and Company (Australia), Limited. 10" x 6", pp. 574. Price: 52s. 6d.

This third edition of "The Physician's Index of Australia and New Zealand" is a useful volume. It is essentially a book of reference. The section of the book which will be of most use to practitioners is that headed "Physician's Index". This is an alphabetical index of ethical preparations available in Australia and New Zealand. It covers some 340 pages and appears to be complete. Substances indexed for the first time are indicated by a special mark. Attention should also be drawn to the section dealing with the British Pharmacopoeia, 1953. Here are set out the additions, deletions and alterations in titles.

**Sex, Society and the Individual: Selected Papers, Revised and Brought Up to Date, from "Marriage Hygiene" (1934-1937) and "The International Journal of Sexology" (1947-1952).** Edited by A. P. Pillay, O.B.E., M.B., B.S. (Bombay), and Albert Ellis, Ph.D. (New York); 1953. Bombay: The International Journal of Sexology. Sydney: Angus and Robertson, Limited. 9" x 6", pp. 458, with 28 illustrations. Price: 56s.

This book consists of a series of chapters reprinted from *The International Journal of Sexology*. There are 45 chapters by various authors. Some authors have contributed more than one chapter and they are divided into six sections. The sections are as follows: "Sex Disorders and Problems", "The Organism Problem", "Sex Offences and Sex Offenders", "Sex in Literature", "Sex Deviations", "Research and Miscellaneous Papers". Those who are specially interested in the subject of sex will no doubt find something in this volume which they will appreciate.

**World Medical Periodicals.** Prepared under the auspices of a committee jointly sponsored by the United Nations Educational, Scientific and Cultural Organization, and the World Health Organization; 1953. Paris: United Nations Educational, Scientific and Cultural Organization. Geneva: World Health Organization. 9½" x 6½", pp. 254. Price: 12s. 6d.

This book, which has been prepared under the auspices of a committee jointly sponsored by the United Nations Educational, Scientific and Cultural Organization and the World Health Organization, will be of the greatest value to all medical libraries. It provides a guide to the world's current periodicals in the medical and biological sciences. It contains the titles of all current medical periodicals which have been traced, all medical biological periodicals regularly surveyed by certain abstracting agencies, and the well known journals which ceased publication during the period 1900 to 1950. Titles of periodicals devoted to pharmacy, odontology and veterinary science are included. Each of the 4000 entries gives the title, place of publication, language or languages of publications (if not apparent from the title), frequency of publication, together with symbols indicating which of the principal abstracting services regularly survey the journal, and, finally, an abbreviation of the title based upon the code rules introduced by the World List of Scientific Periodicals as modified by the International Organization for Standardization.

**Medical Terms: Their Origin and Construction.** By Ffrangcon Roberts, M.A., M.D., F.F.R.; 1954. London: William Heinemann (Medical Books), Limited. 7½" x 5", pp. 96. Price: 6s.

This small book by Ffrangcon Roberts is interesting and useful. It will be specially useful to medical practitioners who have no knowledge of the classics. It is, as the author explains in the preface, not a dictionary in the ordinary sense of the term. In the first part of the book he gives the origin of medical words and the principles of their construction. The second part is modelled on "Roget's Thesaurus" and brings together synonyms and antonyms so as to show how words are related by resemblance, contrast, and shades of meaning. In the introduction, the author has something to

say about the unthinking acceptance of words, looseness of expression and etymological errors. There are chapters on the sources of medical words, the persistence of primitive conceptions, the principles of derivation, and word construction. This book will be of considerable interest to those who are interested in words and their origin.

## Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"The Year Book of the Eye, Ear, Nose and Throat (1953-1954 Year Book Series)"; The Eye, edited by Derrick Vail, B.A., M.D., D.Oph. (Oxon.), F.A.C.S., F.R.C.S. (Hon.); The Ear, Nose and Throat, edited by John R. Lindsay, M.D.; 1954. Chicago: The Year Book Publishers, Incorporated. 8" x 5½", pp. 456, with 126 illustrations. Price: \$6.00.

One of the Practical Medicine Series of Year Books.

"Anatomy for Surgeons: Volume I: The Head and Neck", by W. Henry Hollinshead, Ph.D.; 1954. New York: Paul B. Hoeber, Incorporated, Medical Book Department of Harper and Brothers. 10½" x 7½", pp. 572, with 326 illustrations. Price: \$12.00.

This is the first of three volumes, and is divided into nine chapters.

"Problems of Consciousness: Transactions of the Fourth Conference, March 29, 30 and 31, 1953, Princeton, N.J.", edited by Harold A. Abramson, M.D.; 1954. New York: Josiah Macy Junior Foundation. 9" x 6½", pp. 178, with three text figures. Price: \$3.25.

The subject is discussed by 28 persons.

"Secret Enemy: The Story of a Disease", by James Cleugh; 1954. London: Thames and Hudson. Sydney: Walter Standish and Sons. 8½" x 5½", pp. 278. Price: 18s.

Deals with the history of syphilis.

"Rorschach Responses in Old Age", by Louise Bates Ames, Ph.D., Janet Learned, Ph.D., Ruth W. Métraux, M.A., and Richard N. Walker, M.A.; 1954. New York: Paul B. Hoeber, Incorporated, Medical Book Department of Harper and Brothers. 9½" x 6½", pp. 244, with three text figures. Price: \$6.75.

The present authors made a systematic report on "Child Rorschach Responses"; this volume, dealing with the other end of life, is comparable with that report.

"A Handbook of Diseases of the Skin", by Herbert O. Mackey, F.R.C.S.I., L.R.C.P.I., D.P.H. (Univ. Dub.), L.M., F.R.I.A.M.; Second Edition; 1953. London: Macmillan and Company, Limited. 9" x 5½", pp. 254, with 142 illustrations. Price: 7s. 6d.

Intended primarily for students.

"The Public Health Inspector's Handbook (formerly The Sanitary Inspector's Handbook): A Manual for Public Health Officers", by Henry H. Clay, F.R.San.I., F.I.S.E., assisted by Ronald Williams, O.B.E., D.P.A., F.R.San.I.; Eighth Edition; 1954. London: H. K. Lewis and Company, Limited. 8½" x 6", pp. 628, with 101 illustrations. Price: 30s.

The first edition was published in 1933.

"The Physiopathology of Cancer: A Treatise for Investigators, Physicians and Students", edited by Freddy Homburger, M.D., and William H. Fishman, Ph.D., with a foreword by C. C. Little; 1953. New York: Paul B. Hoeber, Incorporated, Medical Book Department of Harper and Brothers. 10" x 7½", pp. 1050, with 152 illustrations. Price: \$18.00.

There are four parts to this book headed: "Biology", "Chemistry and Physics", "Clinical Investigation", and "Practical Applications". There are 28 contributors.

"Experimental Surgery: Including Surgical Physiology", by J. Markowitz, M.B.E., M.B. (Tor.), Ph.D., M.S. in Exp. Surg. (Minn.), in collaboration with J. Archibald, D.V.M., M.V.Sc., and H. G. Downie, D.V.M., M.S. (Cornell), M.V.Sc.; Third Edition; 1954. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 9" x 6½", pp. 864, with 554 illustrations. Price: £5 7s. 6d.

Best writes in the foreword that Markowitz's approach in this book is the result of all his experiences.

## The Medical Journal of Australia

SATURDAY, JULY 3, 1954.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those adopted by the *Quarterly Cumulative Index Medicus*. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

### THE NEXT CONGRESS.

SINCE the organization of the Australasian Medical Congresses was undertaken by the Federal Council of the British Medical Association in Australia, these gatherings have become firmly established in the corporate life of the medical profession. They provide a meeting ground for the whole profession; here general practitioners, practising specialists, laboratory workers and university teachers can meet together, get to know one another and talk about the latest developments in the medical sciences. It cannot be too strongly emphasized that the congresses are not concerned with medico-political questions. They are organized by the British Medical Association, whose primary object is the study of the medical sciences. Anyone who cares to look back over congresses which have been held since the first took place in Melbourne in 1923 under the presidency of the late George Adlington Syme, will realize that the advances made in the different spheres of medicine have been discussed from many angles at these congresses. Since 1923, many specialist bodies have been formed. This was only to be expected in view of the tremendous strides that have been made in the different specialist spheres. These specialist bodies and groups hold their own annual meetings at which subjects are often discussed on a plane which would not interest the whole profession. This arrangement is not only understandable, but it is also necessary for the continued development of the special branches. Two facts, however, have to be remembered. The first is that there is a general substratum of knowledge which is common to all graduates in medicine and on which every specialized subject or group of subjects is based. This substratum of knowledge is best discussed by the profession as a whole. The second fact is that members of special groups have a duty to all other groups—they have to make all other members

of the profession outside their own group at least aware of what is taking place in the specialized sphere. If this is not done, medicine will develop into a series of separate pockets and the general outlook of medicine will be obscured. More than this, the general practitioners who attend congresses have something to give to members of special groups. They, more than any others, have, *inter alia*, to keep before the whole profession the need for awareness of the patient's environment. The patient cannot be adequately treated apart from his environment, and it is the general practitioner who sees the patient in his home and learns to understand him as a man as well as understanding him as a sick person. This may, at first sight, sound a little far-fetched, but reflection will surely make it clear that it is the doctor who always keeps before his mind the environment of the patient who is the successful practitioner. Success here, of course, is referred to in terms of the well-being of the patient, and not in terms of the social standing or financial success of the doctor. The conclusion is therefore justified that the Australasian Medical Congress (British Medical Association) is the concern of every medical practitioner in the Commonwealth, and that every practitioner will be interested in some degree to learn of the arrangements which are being made for the holding of the Ninth Session of Congress at Sydney on August 20 to 27, 1955, in a little more than twelve months' time.

The month of August has been chosen, as is usual, because at that time the University of Sydney will be in vacation and the University has been good enough to make its buildings available for the holding of Congress. As already announced, the Federal Council has accepted the nomination of the Executive Committee of Congress, and Dr. A. J. Collins, the President of the Federal Council, has been appointed President of the Session. The Executive Committee has met on several occasions and a good deal of the preliminary work has been done. Those who have not had a hand in the organization of a session of Congress do not, perhaps, understand that the work has to be taken in hand more than twelve months in advance. The Executive Committee always communicates with the several Branches and invites nominations for the positions of President and Vice-President of the several sections. This all takes a good deal of time, because the persons who are nominated by the Branches are supposed to give an undertaking when they accept an office in a section that they will attend and take part in its proceedings. The sections which are to be formed are as follows: Anaesthesia; Dermatology; History of Medicine; Medicine and Experimental Medicine; Naval, Military and Air Force Medicine and Surgery; Neurology and Psychiatry; Obstetrics and Gynaecology; Ophthalmology; Orthopaedics; Oto-Rhino-Laryngology; Pathology; Bacteriology, Biochemistry and Forensic Medicine; Pediatrics; Public Health and Industrial Medicine; Radiology and Radiotherapy; Rehabilitation and Physical Medicine; Surgery; Tropical Medicine. Each section will hold its own meetings, combined meetings of sections will also be held and several plenary sessions of Congress are being arranged. One important feature will be the presence of the President of the British Medical Association for 1955, Dr. T. C. Routley, of Toronto, Canada. Dr. Routley was for some years Chairman of Council of the World Medical Association.

tion. He visited Australia in 1950 in connexion with the British Commonwealth Medical Conference and attended the Seventh Session of the Australasian Medical Congress in Brisbane. Dr. Routley is a gifted and forceful speaker; he will deliver the Henry Simpson Newland Oration at the Ninth Session. In another place in this issue under the heading of "Congress Notes" will be found some instructions to those who desire to present papers; a list of the honorary secretaries of sections is also given.

In drawing the attention of readers to this Congress, we would remind them that the interval between Australasian Medical Congresses has been extended to three years—the Sixth Session was held at Perth in 1948, the Seventh at Brisbane in 1950, and the Eighth at Melbourne in 1952. The longer interval between sessions of Congress is, in the opinion of most people, wise, and we shall probably find by August, 1955, that members of the Branches will be quite prepared to meet together once more, especially as no congress has been held in Sydney since 1929. Most medical practitioners plan their absences from practice well in advance, and it is not too early to arrange to attend the Sydney Congress in August, 1955. Members of the Branches are urged to try to include a journey to Congress among their doings for 1955. Honorary local secretaries have been appointed in the several States as follows: New South Wales, Dr. M. S. Alexander; Victoria, Dr. C. H. Dickson; Queensland, Dr. D. A. Henderson; South Australia, Dr. L. Bonnin; Western Australia, Dr. S. E. Craig; Tasmania, Dr. K. S. Millingen. Their addresses are given in the "Congress Notes". Members are requested to apply for application forms for membership to the local honorary secretaries in their own States. The honorary secretary of the Session is Dr. J. G. Hunter, 135 Macquarie Street, Sydney.

## Current Comment.

### VISUAL HAZARDS OF NIGHT DRIVING.

SPECTACLES with tinted glass are sold freely in all manner of shops in a remarkable variety of colours and designs and are worn gaily on all manner of occasions, either for visual comfort or for effect, which the onlooker may or may not find aesthetically acceptable. This indiscriminate use of tinted spectacles has produced a number of problems, including increased hazards associated with night driving. In the United States the last-mentioned situation has been further aggravated by the use of tinted glass in motor-car windscreens. Fortunately, motor-cars in Australia, other than a few specially imported models, have not as yet acquired this refinement, but it is as well that we should be warned in advance. The use of tinted glasses in spectacles offers a more immediate problem, since it is clear from a recent article by Paul W. Miles<sup>1</sup> that tinted glass in windscreens or spectacles brings the possibility of accident due to reduced visual efficiency at night. We should be glad that we are, at least for the present, free from the particularly unfortunate situation described by Miles which arises from the popular selection of pink for the glasses and aquamarine green for the windshields—while pure red and pure green filters may be quite transparent, in combination they are opaque. Miles proceeds to discuss the question of adaptation of vision to night driving conditions and the influence of glare, as well as of looking through tinted glass. He states that when

a person first walks into a dark moving picture theatre, he can see the screen very well, but there is poor visibility of the seats until dark-adaptation has occurred. Night driving is a similar visual task, except that dark-adaptation can never take place. The driver's eyes become adapted to the average amount of headlight reflected from objects on and about the road. The intensity of illumination is such that his vision does not pass over to a state of dark-adaptation. The eyes remain in the photopic state (that is, they are adapted to light as opposed to dark) with adaptation for an intensity of at least 0.1 millilambert, the point at which rod dark adaptation is normally just beginning. Miles points out that at this level the seats in a dark theatre would remain forever black against black, just as the objects at a distance or in the shadow appear on the road. As the driver studies the road at the distance limits of the headlights, he constantly tests his visual thresholds. Objects come into view, attract attention and are finally identified as the motor-car rapidly approaches. "Under threshold conditions, an image may form on the retina 50 times and be so weak that only 25 attention responses follow." Any decrement in the illumination or visual efficiency during high speed night driving could delay reaction enough to result in serious accident.

Of colours used for tinted glass, green is a particularly unfortunate choice, but it is the one usually adopted for tinted windscreens because a green filter cuts out the red and infra-red rays which carry heat from the sun during the day. At night, this colour produces an unbalanced view of the headlight. Almost two-thirds of headlight energy is concentrated in the red end of the spectrum and only one-third is in the range to which a green windscreen is most transparent. Miles produces from available basic data exact figures on visual efficiency when the driver looks through tinted glass during night driving. With clear crown glass there is an 8% loss of transmission of light, this loss being almost entirely by reflection from the two surfaces; so that thickness is not very important. The use of glass of a light shade of yellow, which has enjoyed some popularity as a night driving glass, reduces the average transmission under night driving conditions to 88.4%. With a popular shade of pink glass the average transmission is only 74%. With green windshield glass, the average transmission is as low as 62.4%. With a combination of pink glasses and green windscreen the average transmission drops to 46.5%, the combination being regarded as a dark filter. Apparently the occurrence of this combination at night on American highways is not at all rare. With reduced illumination, as when the headlights are turned down or when the intensity is diminished by mud or mechanical defect, the position is bound to become even more dangerous, the transmission being decreased to 82.8% for yellow glass and to 71.8% for pink glass. There are individual differences, but they are unimportant except in the case of true colour-blindness, when the hazard is greatly increased. Apparently even the slightest tinted glass adds to the visual problem at night for colour-blind persons.

Turning to exact measurements of the visual acuity under night driving conditions, Miles states that with clear crown glass this is 20/32, with yellow glass 20/34, with pink glass 20/40, with a green windscreen 20/46, and with a combination of pink glass and green windscreen 20/60. He states that although these studies were made in the absence of glare, the presence of glare during night driving would not invalidate them. There is no evidence that colour filters improve visual acuity under ordinary night driving conditions with glare from oncoming motor-cars. They may improve comfort and reduce fatigue. These figures were obtained under experimental conditions that must be regarded in some ways as ideal. Miles points out that in the real situation visual efficiency is decreased by object movement, dust, rain, jolting car movements, fatigue, boredom, alcoholism and various distractions; but these, he believes, would only add to the significance of his figures.

Discussing the effect of glare on visual acuity, Miles states that complaints from glare in night driving are

<sup>1</sup>Arch. Ophth., January, 1954.

commoner in persons who have colloidal changes in the ocular media, either from disease or from old age. In such eyes, incoming light rays are scattered by dispersion in the familiar Tyndall phenomenon. A similar dispersion with consequent loss of vision is observed when an oncoming headlight strikes a slightly muddy windscreen at night. Theoretically, dispersion provides a reason for the use of light yellow night driving glasses. Since dispersion is inversely proportional to the fourth power of the wave-length, about sixteen times more blue light rays are scattered in the ocular media than red. A yellow filter should remove the blue light and prevent some of the confusion. In practice, however, the light from automobile headlights is red in colour and contains so little blue that a light yellow filter probably makes little difference. For a similar reason there is apparently not much importance to be attached to difficulties otherwise associated with blue light and chromatic aberration. Miles refers to a number of other poorly understood phenomena which may explain the wide subjective improvement in comfort and in visual acuity reported from the use of light yellow night driving glasses. He concedes that some function of vision may be improved, but not visual acuity.

Thus, it seems clear that the use of tinted glass in automobiles, whether in spectacles or in windscreen, is dangerous because of decreased visual efficiency at night. It interferes not only with visual acuity, but with resolving power. Miles states that a pair of objects would appear separate at 100 feet through a clear windscreen, yet would appear single through a green windscreen until the distance had decreased to 25 feet. A great many other factors of vision are likewise found to be defective in night driving conditions with tinted glass. Miles's final recommendations may be noted with interest, though they are not all particularly relevant to Australian conditions. He suggests that green windscreen glass, if used, should be in a separate layer so that it can be moved aside for night driving. Persons with defective vision, including those with colour-blindness of the common type, should be advised to add auxiliary headlights to their motor-cars and to avoid any type of tinted glass for night driving. Finally, since glare is inversely proportional to the area of the source, automobile headlights should be designed larger in area.

#### TREATMENT OF LUPUS ERYTHEMATOSUS WITH MEPACRINE.

IN 1950, as the result of a chance observation, Francis Page<sup>1</sup> at the Middlesex Hospital, London, used mepacrine in the treatment of a patient suffering from *lupus erythematosus*. The response was so dramatic that the treatment was continued, and in 1951 Page published "with hesitation" (being aware of the fallacies associated with any new remedy for a chronic relapsing disorder) the results of this form of treatment in 18 cases. In only one had the patient shown no improvement. In a few cases all the lesions had completely disappeared within six weeks of starting treatment, with the result that it was no longer possible to distinguish their previous sites. One patient suffering from acute disseminated *lupus erythematosus* had been treated with success. In two cases associated changes of rheumatoid arthritis had disappeared as the skin condition had improved. This appears to have been the first report in English-speaking countries of the treatment of *lupus erythematosus* with mepacrine, and Page was apparently not aware that reports on the use of this form of treatment had appeared in European Continental journals over the previous ten years. However, the treatment was taken up in both Britain and the United States and a number of reports have subsequently appeared. There seems to be general agreement that mepacrine is effective in the treatment of chronic discoid *lupus erythematosus*, though experience in its use with systemic *lupus erythematosus* has been less satisfactory. This general

experience is exemplified in the results reported last year to the seventy-third annual meeting of the American Dermatological Association by Robert R. Kierland, L. A. Brunsting and P. A. O'Leary.<sup>1</sup> Following the suggestions of Page, they treated with mepacrine 60 patients suffering from *lupus erythematosus*; fifty-five had the chronic discoid form of the disease and five had moderate systemic manifestations. The dosage used was 100 milligrammes of mepacrine hydrochloride three times a day for the first week, twice a day for the second week and then once a day as long as was necessary. Only eight of the patients had received no previous treatment. The others had had many types of therapy, including gold, bismuth, arsenic, quinine, iodides, vitamins B, B<sub>12</sub> and E, liver extract, carbon dioxide snow, cortisone, corticotrophin, androgens, oestrogens and local preparations. In presenting their results, Kierland, Brunsting and O'Leary state that in appraisal of the results it is apparent that the only parts of the skin lesion that can be expected to show a favourable response are the erythema and the inflammatory infiltrate. It is not expected that the scars will change. Of the 52 patients who were followed up, 11 were classed as 0% to 25% improved, nine as 25% to 75% improved, 15 as more than 75% improved but without arrest of the disease, and 17 as having complete arrest of the disease. Several patients who had been receiving low maintenance doses of 50 to 100 milligrammes of mepacrine daily noted that after exposure to the sun in the spring some of the lesions of *lupus erythematosus* again became active after several months of inactivity. The recurrent lesions were found most often on the lower lip, lobe of the ear and nose. Lichenoid eruptions appeared in some cases, but none of the patients had any of the serious sequelae from mepacrine noted in World War II, such as followed the New Guinea variety of lichenoid dermatitis—namely, alopecia, hyperpigmentation, anidrosis or scarring. Leucopenia developed in one case. Altogether, these investigators were satisfied from their experience that administration of mepacrine is of great value in the treatment of the chronic discoid types of *lupus erythematosus*, and at the same time the incidence of untoward reactions is low. On the other hand, they consider that therapy with mepacrine in cases of systemic *lupus erythematosus* is hazardous. In all five cases of this type in the series untoward reactions developed, although three of the patients had experienced benefit from the treatment before the undesirable incident occurred. This has not been the universal experience, as other investigators have made favourable reports on the treatment of systemic *lupus erythematosus* with mepacrine, and it was suggested in the discussion that followed the presentation of this paper that the solution to the difficulty might lie in adjustment of dosage. However, in any case, Kierland, Brunsting and O'Leary recommend that erythrocyte and leucocyte counts, as well as haemoglobin estimation, should be carried out frequently while the patient is under treatment with mepacrine. So far as patients with the chronic discoid form are concerned, the danger of untoward reactions appears to be small and the possibility of benefit very considerable.

#### INTERLINGUA.

It is the custom for some of the more specialized medical journals, which have a world-wide circulation, to publish the summaries with which original articles usually conclude, in two or more languages. An international language would be admirable for this purpose, and in the January, 1954, issue of *Blood* the practice has been inaugurated of printing these summaries in "Interlingua", a new "supranational" language which has been brought into use by "Science Service" of New York. In an editorial William Dameshek writes that it had been felt for a long time that it was not sufficient to print summaries of articles in *Blood* in English alone. The question was, which languages should be used. The increasing awareness of Latin-America

<sup>1</sup> *Lancet*, October 27, 1951.

<sup>1</sup> *Arch. Dermat. & Syph.*, December, 1953.

in the United States had led some journals to print summaries in Spanish, but this was not of much help to the Brazilians, who used Portuguese, to the Haitians or to the many French-speaking Canadians. Interlingua seemed to offer a solution of the problem of "which language".

Interlingua is, of course, by no means the first of the international languages, but Dameshek thinks that it may succeed where others have failed. It is based on the idea, developed chiefly by an Austrian, Julius Lott, and a Chilean surgeon, Alberto Liptay, that "the international language does not need to be invented. It exists. One only needs to collect all its words and set them in order". The summaries in *Blood* have been compiled with the help of the Interlingua Division of Science Service and of Dr. Alexander Gode of New York. According to the latter, Interlingua "aims to be simultaneously French, English, Spanish, Italian, and so on", each one of these languages being used according to a set plan. The plan, briefly, is that for a word to be classified as international it must be used in at least three of these languages, with German or Russian as possible substitutes. All users of the "Romance" languages should be able to read Interlingua with ease, though they will feel that someone has been taking liberties with grammar and construction. An Englishman or an American may find it a little difficult at first unless he has a fair knowledge of Latin or of Spanish or Italian. Interlingua is primarily extracted and amalgamated out of Italian, French, English, Spanish and Portuguese combined, but as it develops it is expected that German, Russian and the various Oriental languages will contribute to it as they have done and are doing to English and other languages.

Here follows a sample of Interlingua:

#### *Summario in Interlingua.*

Un caso de neutropenia periodic de un duration de vinti annos es presentate. Administration intravenose de ACTH esseva empleate in le spero de facer abortar o de prevenir le cyclos neutropenic. Nulle effecto in altiar le conto total de leucocytes o neutrophilas esseva constatate, e le cyclos neutropenic non poteva esser prevenite per medio de ACTH. Un frappante absentia de febre, stomatitis, e altere manifestationes secundari esseva notate durante le periodos de therapia a ACTH. Etiam le conditiones governante le tractamento hormonico de tal casos es discutate.

The English summary is as follows:

#### *Summary.*

A case of periodic neutropenia of twenty years' duration is presented. ACTH was administered intravenously in an attempt to abort or prevent the neutropenic cycles. No effect in raising the total leukocyte or neutrophil count was noted, and the neutropenic cycles could not be prevented by the ACTH. A striking absence of fever, stomatitis, or other secondary manifestations occurred during the neutropenic periods treated with ACTH. The background for treating such conditions with hormones is discussed.

### THE TREATMENT OF TUBERCULOUS MENINGITIS.

THE introduction of streptomycin in 1947 was a landmark in the treatment of tuberculous meningitis. John Lorber<sup>1</sup> describes four main stages in the treatment since then. In the first stage, in 1947, streptomycin alone was available "and no one knew the best way to use it". In the second stage, from 1948 to 1950, streptomycin treatment was more standardized, and consisted in prolonged and uninterrupted intramuscular courses with shorter and often interrupted intrathecal courses. Various refinements of administration and adjuvants of debatable value were introduced. Towards the end of the period, intrathecal tuberculin therapy was introduced. The third stage was

characterized by the routine oral administration of PAS and the selective intrathecal use of tuberculin in conjunction with streptomycin treatment. The fourth stage, which still continues, began with the introduction of isoniazid in April, 1952. Lorber briefly reviews the results obtained in the first two of these stages and, using these results as a base line, goes on to describe his experience in the treatment of children suffering from tuberculous meningitis with streptomycin and PAS. The series consisted of 38 children admitted to hospital between August, 1950, and March, 1952. They were given streptomycin by the intramuscular and the intrathecal routes and PAS by mouth. Twelve selected patients with a poor prognosis were given intrathecal tuberculin therapy. Comparison of the results with those obtained with previous systems of treatment show considerable improvement. Of 27 children who were conscious on admission to hospital, 25 recovered, and the two deaths were not due to tuberculous meningitis. Of 11 children admitted with advanced tuberculous meningitis, only three survived, and two had severe sequelae. Despite this group of bad results, nearly three-quarters of the whole series of children survived with a minimum period of observation of two years from the beginning of the treatment and thirteen months from the end of the treatment. It is interesting to note that apart from the increased survival rate, the condition of the survivors was better, more have been free from sequelae, and fewer have become decerebrate than in previous series. There have been no late deaths. The age of the children appeared to have an influence on the prognosis, as the survival rate amongst those aged less than three years was considerably less than amongst those aged more than three years. However, more careful consideration of the facts shows that these worse results were directly due to delay in diagnosis and were not related to the age of the children *per se*. Young children who were conscious on admission to hospital did as well as older children; and it is very clear that all possible efforts must be made to avoid delay in diagnosis, so that children may be admitted to hospital while they are still conscious if the best results are to be obtained.

Lorber states that increasing experience undoubtedly played a part in the improvement in the results, but the outstanding difference is the elimination of deaths after the second month of treatment. The prevention of the development of streptomycin-resistant organisms by the adjuvant action of PAS was probably responsible for this. No resistant organisms were found in this series. Intrathecal tuberculin therapy appeared to benefit three children who were in the intermediate stage on admission to hospital and who did not respond to routine treatment, but the results indicate that the routine use of intrathecal tuberculin therapy is not justified. Lorber states that intrathecal treatment with streptomycin has not been continued until the cerebro-spinal fluid has returned to normal. Indeed, the cerebro-spinal fluid usually did not return fully to normal for from nine to fifteen months with this method of treatment. So long as the cerebro-spinal fluid showed a steady tendency to improve, it did not seem to matter and did not lead to late deaths. The policy spares the patient much pain and reduces the risk of deafness.

Lorber acknowledges the possibility that a further reduction of intrathecal treatment may not be reflected in poorer results now that isoniazid is available, but the risks involved in disregarding the good results with the method described may be serious and need careful consideration before any further modification is made.

Lorber has given his results with isoniazid in a separate report.<sup>1</sup> This describes a series of 22 patients suffering from tuberculous meningitis who were conscious on admission to hospital and were allocated by random sampling to two treatment groups; ten were treated as controls and twelve were given isoniazid. The treatment otherwise was identical in the two groups, intrathecal streptomycin treatment being given in all cases. Eight of the ten controls and eleven of the twelve isoniazid-treated patients survived. The average period of observation was seventeen months for the controls and fourteen months for the isoniazid

<sup>1</sup> *Lancet*, May 29, 1954.

<sup>1</sup> *Lancet*, June 5, 1954.

group. None of the patients have serious sequelae, and none are deaf. It should be noted that patients in the isoniazid group required fewer intrathecal injections of streptomycin (the average was 65) compared with the controls, for whom the average was 90. In general, the cerebro-spinal fluid in the isoniazid group approached normal more rapidly than in the other group, but it showed significant deterioration in six children after one course of intrathecal treatment had been completed, and so further intrathecal streptomycin treatment was required. Tubercle bacilli reappeared in the cerebro-spinal fluid of one child during isoniazid treatment.

It is apparent from this small series that the addition of isoniazid to streptomycin and PAS has produced no significant increase in the survival rate. Lorber points out, quite reasonably, that this may be partly explained by the high survival rate in patients treated without isoniazid; one would require much larger numbers to demonstrate small improvements in this respect. The important point is that the same survival rate was achieved with fewer intrathecal injections, and it may be possible to reduce the number and frequency of intrathecal injections further without impairing results. This would have obvious advantages and the problem is under investigation at present. Discussing the question of whether intrathecal treatment is necessary at all, Lorber concedes from the work of others that many patients with tuberculous meningitis recover without intrathecal treatment. He points out, however, that the object must be to cure the highest possible number of patients, and it has not been shown that this can be done without intrathecal treatment; thus, it would seem unwise, on the present evidence, to depart from a regime whose effectiveness is established. The present encouraging position seems to be that with intramuscular and intrathecal streptomycin therapy (the latter being reduced in amount but not eliminated by the additional use of isoniazid) and oral PAS therapy, the chances of death of the patient from tuberculous meningitis are very small provided that he is conscious when treatment begins.

#### PERNICIOUS ANÆMIA AND CANCER OF THE STOMACH.

In the last ten years considerable evidence has accumulated to show that pernicious anæmia predisposes the subject to cancer of the stomach. In post-mortem studies H. S. Kaplan and L. G. Rigler (1945)<sup>1</sup> found that cancer of the stomach occurred in 12.3% of individuals who had had pernicious anæmia; this was more than three times the incidence in those who had not suffered from this disease. J. Mosbech and A. Videbaek (1950)<sup>2</sup> showed a similar high incidence of gastric cancer in 301 pernicious anæmia patients followed for an average of 10.5 years. However, the total mortality and the mortality from cancer in their series was the same as that expected in a comparable group of the general population. So that, of all cancers, cancer of the stomach was unusually predominant and other types had a somewhat lower than normal incidence. Other surveys of malignant tumours associated with pernicious anæmia have shown that the proportion of gastric cancers is two or three times that normally occurring.<sup>3,4</sup> Another unexplained feature is that the increased incidence of gastric cancer among pernicious anæmia patients is more marked for males than for females.

Various hypotheses have been advanced to account for the association of these two diseases. It is unlikely that cancer of the stomach causes pernicious anæmia, as has been suggested, by destruction of the mucosa, since total gastrectomy rarely leads to such a complication. Pernicious anæmia, however, often precedes the development of gastric cancer by several years. So that it is likely either that the former disease or a concomitant of it is a precursor of the latter or else that there may be a predisposing factor

common to both. Pathological changes in the stomach of pernicious anæmia patients, in particular chronic atrophic gastritis, have been indicted as precancerous. However, not only is the atrophic gastritis localized primarily to the fundal area and cancer when it occurs not so localized, but also careful studies by L. W. Guiss and F. W. Stewart<sup>5</sup> have shown that chronic gastritis frequently occurs in individuals past middle age and is no more commonly associated with gastric cancer than with other diseases. For the same reason achlorhydria cannot be an important factor in the development of cancer.

The recent work of R. M. Graham and M. H. Rheault<sup>6</sup> on the cytology of gastric contents is relevant to this problem. They found two types of cell—swallowed squamous cells from the oesophagus and upper respiratory tract and columnar cells from the gastric mucosa. Both types showed abnormalities in patients with untreated pernicious anæmia. The squamous cells were larger than usual, sometimes with multiple nuclei, a result of abnormal mitosis, and the nuclear pattern was irregular with clumping of chromatin. The columnar cells were abnormally large and their nuclei showed an increase in chromatin which was irregularly distributed. Similar abnormalities were not found in anæmia due to other causes, and in pernicious anæmia the cells returned to a normal appearance when patients had adequate treatment with vitamin B<sub>12</sub>. Thus the absence of vitamin B<sub>12</sub> by leading to abnormal mitosis may favour the development of cancer. That there is a long latent interval (during which the patient may be treated) between the discovery of pernicious anæmia and the onset of recognizable malignant disease is no argument against such a view, since a latent period has already been demonstrated for many carcinogens. In the case of workers with  $\beta$  naphthylamine the period was on an average 15.5 years.

Hereditary factors in both pernicious anæmia and cancer of the stomach have been extensively studied by J. Mosbech.<sup>3</sup> He is satisfied that such factors are involved to some extent in both diseases. His aim in a study recently reported<sup>4</sup> was to determine if there was a common inherited factor in the development of both these diseases. To do this, he compared the incidence of gastric cancer in 2881 relatives of 234 patients with pernicious anæmia, with its incidence in 2956 relatives of 225 healthy persons. The two groups of relatives were uniform in sex ratio and age distribution, and the investigation was made in the same manner for both. In a similar proportion of cancer cases in each group the diagnosis was verified by death certificates, hospital records or necropsy. A gross difference was found in the number that had died from cancer of the stomach in the two groups—108 in the pernicious anæmia relatives, 33 in the control series. Cancer of the oesophagus and at other sites was also more common in the former, though the difference was less marked. However, the number of deaths from cancer of the stomach which might have been expected from mortality statistics is 79.8 in the pernicious anæmia relatives and 75.2 in the controls. Thus, though the actual mortality in the pernicious anæmia series remains significantly greater, it does not seem so excessive. Mosbech cannot explain why the incidence of cancer in the stomach and at other sites is considerably lower in the control series than the calculated incidence, but he nevertheless considers that his control series forms the proper basis for comparison. Perhaps this discrepancy may be explained if a considerable proportion of people with gastric cancer have relatives with pernicious anæmia; but this remains to be demonstrated.

Mosbech suggests that since no external cause could be found for the higher incidence of gastric cancer in pernicious anæmia relatives, an hereditary factor should be considered. Thus gastric cancer in pernicious anæmia patients and their relatives may be determined, in part, by an inherited factor which predisposes them to both these diseases. If this is true, then environmental influences may decide whether either or both occur in any particular patient.

<sup>1</sup> *Am. J. M. Sc.* (1945), 209: 339.

<sup>2</sup> *Brit. M. J.* (1950), 1: 390.

<sup>3</sup> *Lancet* (1949), 1: 249, 291, 336.

<sup>4</sup> *Hæmatologica* (1938), 19: 939.

<sup>5</sup> *Arch. Surg.* (1943), 46: 823.

<sup>6</sup> *J. Lab. & Clin. Med.* (1954), 43: 235.

<sup>7</sup> "Heredité in Pernicious Anæmia" (1953), Copenhagen.

<sup>8</sup> *Acta med. Scandinav.* (1954), 148: 210.

## Abstracts from Medical Literature.

### RADIOLOGY.

#### Right Cardio-Phrenic Angle Masses.

JAMES V. ROGERS, JUNIOR, AND TED F. LEIGH (*Radiology*, December, 1953) state that the diagnosis of many right cardio-phrenic angle masses can be established with reasonable certainty by radiographic procedures. The smaller congenital pericardial cyst or diverticulum usually has a characteristic "tear-drop" configuration in the lateral view, which serves to identify it. An ommental herniation through the right foramen of Morgagni can nearly always be identified by the elevation of the transverse portion of the colon and by the presence of air in the hernial sac following pneumoperitoneum. Large pericardial cysts and diverticula, and hernial sacs which fail to fill with air because of adhesions obliterating the neck of the sac, cannot be diagnosed with certainty by X-ray procedures alone. In these cases, a cystic structure may be suspected if definite changes in shape occur with respiration. Ommental herniae may be suspected if there are alterations in the position of the transverse colon.

#### Rib Notching in Congenital Heart Disease.

J. V. KENT (*Brit. J. Radiol.*, July, 1953) refers to those conditions which may be associated with notching of the ribs. He states that in Fallot's tetralogy a mechanism is known to exist by which such changes rarely occur. An account is given of two cases of congenital heart disease in which the rib lesions were produced by an entirely different mechanism. The chief feature of these cases was that the rib notching, absent before operation, appeared only on the side of thoracotomy after division of the sub-clavian artery, a step in the Blalock pulmonary-systemic anastomosis. It is concluded that the erosions developed as a result of the participation by the intercostal arteries in a collateral circulation to the arm. Angiocardiographic studies supported this conclusion. The author concludes that it is unlikely that these cases are unique.

#### Radiography of the Abdominal Viscera.

ANTONIO GOVONI, JAMES F. BRILSFORD AND ERIC H. MUCKLOW (*Am. J. Roentgenol.*, February, 1954) describe the use of hydrogen peroxide for the elimination of gas from the intestine during radiography of the abdominal viscera. The patient was given an enema at body temperature, the fluid used consisting of 10 cubic centimetres of hydrogen peroxide (40 volumes) per litre of water. This is introduced very slowly, the patient being encouraged to move from the prone position to the left side, to the supine position and to the right side. When the whole of the enema has been introduced the patient lies for a short time on the right side. It is important, however, that the patient should evacuate the enema on the first symptoms of vague abdominal colic, because it was found that if this precaution was neglected the colic was readily followed by a diffuse atony of the colon with a resulting defective elimination of the

gases. The pH of the solution is about 7 (measured with the bromthymol method). The hydrogen peroxide may act by producing a neuro-muscular excitation of the colon, which stimulates evacuation of its contents, and perhaps to a minor extent, by increasing the tension of the colon, may lead to a quicker transfer of the gas from the colon to the blood. To ensure success with this method attention should be given to the diet for the two days preceding the examination, such things as legumes being excluded in order to ensure a low residue in the colon. Further, the disturbing effects of air swallowing should be explained to the patient and his attention sought in avoiding it. Hydrogen peroxide can usefully be employed, in the concentration suggested, in the barium enema used for visualization of the colon. With it, effective evacuation of the bowel occurs and a very good mucosal pattern of the whole colon is secured in which relatively small localized irregularities can be detected. It has all the advantages of tannic acid with none of its disadvantages.

#### Metabolic Craniopathy.

HOWARD B. APPELMAN AND ROBERT C. MOEHLIG (*Am. J. Roentgenol.*, March, 1954) report two cases of metabolic craniopathy (*hyperostosis frontalis interna*) with concomitant osteopolkilosis in a mother and daughter. They present strong evidence for the hereditary nature of osteopolkilosis and the sex-linked hereditary nature of metabolic craniopathy, the latter probably being inherited as a dominant trait. A metabolic disturbance associated with pituitary dysfunction is apparently responsible for *hyperostosis frontalis interna*. The symptoms are in part due to the pituitary dysfunction and in part to pressure resulting from the *hyperostosis frontalis interna*. The authors discuss the history, aetiology, pathology and symptomatology of both conditions, and conclude that, although the most plausible theory for osteopolkilosis is that of a congenital *Anlage*, it is possible that it, too, may be due to a pituitary dysfunction.

#### Strangulating Obstructions of Small Intestine.

HARRY Z. MELLINS AND LEO G. RIGLER (*Am. J. Roentgenol.*, March, 1954) state that the X-ray diagnosis of strangulating obstruction may be missed if the entity is not specifically sought or if one considers that there is a single sign which should be present in every case. Strangulation obstruction is produced by a fairly constant anatomical derangement, the incarcerated or twisted intestinal loop. This, however, initiates physiological disturbances which are progressive or changing in character, and varying radiological signs mirror the various phases of the pathological process. The evidence of an incarcerated loop may be of two types. If the loop is only partially closed, it will be gas filled or gas and fluid filled. In the horizontal film gas will be seen in the two distended limbs of the incarcerated loop. The gas shadows will be separated by the apposed intestinal walls, probably somewhat edematous, and therefore producing a thicker shadow than normal. This has been called the "coffee bean" sign. If the incarcerated loop is completely closed, it will contain little or no gas. Intestinal gas is either swallowed air (72%), a diffusion

product into the intestines from the blood-stream or the result of intestinal putrefaction. A completely closed loop obviously will not admit the gas which descends from the upper portion of the intestine, and therefore the largest source of intestinal gas is excluded from the incarcerated loop. It will contain, for the most part, only the bloody transudate resulting from the process of strangulation. A small amount of swallowed air may be found in a completely closed loop if the process of closure has developed over a period of time, beginning with a partial obstruction. X-ray films of the abdomen will then show the fluid-filled closed loop as a somewhat rounded or oval-shaped soft-tissue density, the "pseudotumour" sign. While the "coffee bean" sign is harder to distinguish when there is gas in the superior segment of the small intestine, the "pseudotumour" sign is enhanced by the presence of gas in the upper reaches of the small intestine. Fixation of the involved loop is the third of the signs usually observed. Films should be made with the patient in the erect, supine and lateral decubitus positions in order to bring this out. Lack of movement of the loop is strongly in favour of a diagnosis of closed loop obstruction. In the presence of a large amount of gas in the upper part of the small intestine, fixation may be somewhat difficult to determine. Short incarcerated loops will tend to show a higher degree of fixation than longer loops. While the normal small intestine shows a continuing auto-plastic change in the contour and appearance of the *valvulae conniventes*, distended small intestine contains fixed semicircular or circular valvulae. When stagnant anoxia occurs, there is loss of tone of the *muscularis mucosa*, and the fixed valvulae disappear, leaving a smooth or formless intestinal lumen. This sign of strangulation can be demonstrated either within the gas-filled incarcerated loop or within the intestine just above, provided there has been sufficient distension to compromise the intramural circulation.

#### Gas Within Fetus Indicating Foetal Death.

A. F. CRICK AND F. H. SIMS (*J. Fac. Radiologists*, October, 1953) emphasize the importance of gas in the foetal vascular system as a sign of intra-uterine death. They consider that the sign is an early one, is not uncommon and, when it does occur, is pathognomonic. The mechanism of the gas formation is obscure, but the facts that samples subjected to bacteriological examination were for the most part sterile, that in some cases a considerable proportion of the gas disappeared, and that it was substantially nitrogen, all strongly suggest that the gas formation was not due to bacterial activity. The importance of a careful search for the sign and the use of the lateral projection are stressed.

#### PHYSICAL THERAPY.

##### Glandular Cutaneous Cancer.

K. SETÄLÄ (*Am. J. Roentgenol.*, December, 1953) states that certain highly differentiated skin carcinomata contain sebaceous structures, and this paper is an attempt to assess the results of surgery and radiotherapy in these cases. There are two types of dermal gland carcinomata. In the first type

the microscopic architecture and mode of growth resemble those seen in actual dermal cancer, and they react to treatment in the same way. In the second uncommon type there are properties resembling those sometimes seen in cancer of the mammary gland. These properties relate to microscopic appearance, general development of the disease, superficial mode of dissemination (cancer *en cuirasse* type), intra-epidermal proliferation indistinguishable from Paget's disease of the nipple and a tendency to form both regional and distant metastases. The author reviews 33 cases; surgery was used as treatment for the primary or recurrent lesion without irradiation in 13 cases, and in the remaining 20 cases irradiation or irradiation with surgery was employed. Of the 13 cases in which surgery was employed alone, in 10 local recurrence developed and in four metastasis occurred. Of the 20 cases in which previous treatment was given by irradiation, in five the condition recurred locally, two of the patients dying from carcinosis. It is considered that in the cases in which recurrence followed irradiation the dose given was too low. Tumours of the first type on the whole responded to adequate irradiation as well as the ordinary dermal carcinoma. Tumours of the second type responded badly to irradiation, and three cases terminated fatally from metastatic spread. The author concludes that carcinomata of the first type should be treated by irradiation rather than by surgery and should be cured. However, carcinomata resembling those of mammary gland carcinoma in this series were not cured.

#### Secondary Lymph Node Deposits from Pharyngeal Carcinoma.

B. ANTONIAZZI *et alii* (*Brit. J. Radiol.*, March, 1954) present a report based on the results of high-dosage X-ray therapy in a series of 31 cases of secondary cervical lymph node deposits from tumours arising in the pharynx and the base of the tongue. The area irradiated extended from the mastoid to the clavicle, and from the posterior margin of the thyroid to the anterior margin of the trapezius. Average doses of 5000r to 9000r were given over a period of two to four months. In five cases the lymph node involvement persisted, and block dissection was carried out. The only case presenting any difficulty was one in which the patient was operated on one hundred and fifty-five days after irradiation. The other four cases, in which surgery was undertaken ten to eighty days after irradiation, presented no special difficulties. In two of the cases no evidence of viable carcinoma cells was found on histological examination, although clinically glands were still palpable. The authors conclude that: (i) malignant lymph nodes can be successfully treated by irradiation, and this should be employed when radical surgery is contraindicated; (ii) despite high doses, sterilization is often not achieved; (iii) the persistence of palpable lymph nodes after radiotherapy does not necessarily mean that malignant change persists; (iv) radical surgery is always possible after high doses of irradiation, provided that radiotherapy is carefully planned, and as tissue damage increases slowly, surgery if required should be undertaken without delay.

#### Oesophageal Carcinoma.

F. BUSCHE (*Am. J. Roentgenol.*, January, 1954) states that in the last decade both surgical and radiological techniques have been developed which promise more satisfactory results in the treatment of carcinoma of the oesophagus. In a comparison between results the author recognizes four segments in the oesophagus: a cervical segment and three segments of the thoracic part of the oesophagus which is divided into the upper fourth, middle half and lower fourth segments. Surgical removal of cancer in the cervical portion of the oesophagus has proved disappointing. Figures from the Memorial Hospital showed only one patient in seven free of symptoms after five years; whereas at the *Radium-hemmet*, of 56 patients 10 were free of symptoms at the end of five years. The author considers that radiotherapy is the method of choice for treatment in this segment. With cancer of the lower fourth of the thoracic part of the oesophagus the position is quite different. These tumours tend to spread through the cardia and involve sub-diaphragmatic lymph glands, and irradiation of such large areas with high dosage is usually impossible. The five-year surgical results are considerably higher than the few radiological results which are available, reaching 14.8% in one series of 74. The upper and middle segments of the thoracic part of the oesophagus are the origin of about 77% of oesophageal cancers. The five-year survival rates in two large series of cases, treatment in one of which was by radiotherapy and in one by surgery, were very similar, being 3.6% and 2.5% respectively. Analyses of these series shows, however, that the condition of at least one-third of the patients accepted for radiotherapy was too advanced for surgery to be contemplated. The author considers that with increasing experience a better selection of patients can be made, and he points out the results of Garlock, who obtained 10 five-year symptom-free patients in a series of 36. Garlock explored only 46% of the patients seen. The author states that it seems that surgical removal and radiological control of the primary lesion, as long as it is not extended beyond the oesophageal wall, are approximately equal in efficiency. Direct extension through the wall with fixation to the mediastinal structures makes curative surgery impossible, but a small chance of cure by radiotherapy remains. The main cause of failure in both methods, however, is the early formation of metastatic deposits in the para-oesophageal and mediastinal lymph nodes; it is unlikely that improvement in radiotherapeutic techniques can overcome this cause of failure, and the possibility of surgery doing so is not much greater. For the greater number of cases of oesophageal carcinoma the question is one of palliation, and here radiotherapy has much more to offer than surgery. With medium voltage X-ray therapy restoration and maintenance of oral feeding can be obtained in about 50% of cases. With rotation therapy this rises to about 66%, and the strain on the patient to achieve this is less than with any form of surgical procedure. The author considers that when palliation is the aim radiotherapy should be preferred over any form of surgery.

#### MEDICINE.

##### Electrocardiographic Signals by Telephone.

E. G. DIMOND AND F. M. BERRY (*Am. Heart J.*, December, 1953) describe apparatus which they have developed for transmitting electrocardiograms by telephone. The transmitting equipment consists of an ordinary electrocardiograph plugged into a frequency-modulation modulator unit, which converts the low-frequency voltage appearing across the galvanometer to a 1250-cycle frequency-modulated voltage. This is done by employing an oscillator whose frequency may be varied in response to another voltage. The oscillator output is applied to the telephone terminals. At the receiving terminal the frequency-modulated voltage is amplified and applied to a discriminator, which converts the frequency variations to amplitude variations. The output is a voltage identical with that which appeared at the galvanometer terminals of the original electrocardiograph, and it is applied to a galvanometer connected to a writer at the receiving end.

##### Cortisone and ACTH in Cardiac Infarction.

M. P. HOOVER AND G. W. MANNING (*Am. Heart J.*, March, 1954) have found in a series of experiments on twenty dogs that ACTH and cortisone have little or no effect on the healing of experimentally produced cardiac infarction in the dog, and that the use of these substances does not influence in any way the immediate mortality following sudden coronary occlusion in the conscious dog.

##### Purulent Bronchitis Treated with Deoxyribonuclease.

P. C. ELMES AND J. C. WHITE (*Thorax*, December, 1953) have treated acute purulent exacerbations of chronic bronchitis with inhalations of deoxyribonuclease. They have found that the enzyme reduces the viscosity of the purulent sputum but has no effect on mucoid sputum. No change in the course of the disease was observed.

##### Streptomycin and the Fetus.

A. SAKULA (*Brit. J. Tuberc.*, January, 1954) reviews the literature relating to the administration of streptomycin to pregnant women and describes an illustrative case of this. He concludes that streptomycin is innocuous to the fetus when given to the mother in the dosages usually employed, even when given in the first trimester of pregnancy in prolonged dosage and even though the mother may suffer toxic effects.

##### Respiratory Infections Treated with Dihydrostreptomycin Inhalations.

M. KARP *et alii* (*Dis. Chest*, March, 1954) have treated 342 persons suffering from infections of the upper respiratory tract with inhalations of dihydrostreptomycin dust and have found it superior to penicillin inhalations. Patients with bronchiectasis (125 in number) were treated as out-patients for ten days with the aerosol in small disposable units with moderate to excellent improvement in their condition.

## Special Articles for the Clinician.

(CONTRIBUTED BY REQUEST.)

### CIII.

#### TRIGEMINAL NEURALGIA.

##### Causation.

The causation of *tic douloureux* is not known. Harris holds that it is due to neuritis of the terminal twigs of the fifth cranial nerve, secondary to infection of teeth or nasal sinuses. Occasionally pain indistinguishable from true tic is experienced by patients suffering from disseminated sclerosis, and in a few instances fibrous plaques have been demonstrated in close relationship to the sensory nuclei of the fifth nerve.

Tumours and aneurysms in the region of the cerebello-pontine angle occasionally seem to cause pain resembling trigeminal neuralgia. It is suggested by Taarnhoj that compression of the sensory root, as it passes between the postero-superior margin of the petrous temporal bone and the superior petrosal sinus, may be the cause of pain in the majority of cases, and on this assumption he bases his decompression operation.

##### Clinical Features.

Trigeminal neuralgia affects chiefly persons over forty years of age, although rarely it occurs in quite young people. It is more common in females than in males. The right side of the face is affected more frequently than the left. Both sides may be involved in a small proportion of cases. The pain most frequently commences in the lower part of the face, below the line of the eyes, only very rarely above them. It seems to be superficially situated in the cheek, lips or gums, in contradistinction to some other pains which are felt deeply in the face. At first the pain is limited to a rather small area; but as time goes on it tends to spread to other regions, but not beyond the field of distribution of the fifth nerve.

Typically the pain is very severe, sharp and often with an element described by patients as electric. It occurs in spasms lasting a few seconds and recurring at irregular intervals throughout the day and night. This sort of thing may continue for a few days, weeks or months, then come to an end. The patient may then be free of pain for weeks, months or even years, but not permanently. Sooner or later there is another attack; and as time goes on these recur with greater frequency, last longer and increase in severity until the state of the patient is tragic indeed.

During an attack there may often be found on the lips, cheeks or gums small sensitive areas which are known as trigger points. Stimulation of these by touching, movement, as in smiling or eating, washing *et cetera*, is sufficient to precipitate a spasm of pain, and the patient carefully avoids such excitation. He may fear to wash, shave or even take food. For a few minutes after a spasm of pain, stimulation of the trigger point may fail to elicit a response; there seems to be a sort of refractory period, during which preparations are made for the next explosion, which cannot be set off till all is ready. Once a trigger point has been established, it persists throughout subsequent attacks, even though other sensitive spots may arise.

Examination of the central nervous system discloses no abnormality in cases of uncomplicated *tic douloureux*. Mention has been made of the occasional occurrence of similar pain in conjunction with disseminated sclerosis, tumours in the cerebellar fossa *et cetera*. A careful search for signs of organic disease should therefore be carried out.

##### Diagnosis.

When a patient gives a clear story of short spasms of severe pain in the face occurring irregularly in attacks lasting a few weeks, interspersed by long periods of freedom from discomfort, it is almost certain that he is suffering from trigeminal neuralgia. If, on the other hand, he is constantly in pain or has pain for days on end without remission, if the pain spreads beyond the region of the fifth nerve distribution, if it is situated deeply in the face, or if there are no trigger points *et cetera*, then a diagnosis of trigeminal neuralgia should not be made.

In both cases a careful clinical examination must be conducted, special attention being paid to the mouth, nasal sinuses and central nervous system. Radiological examination of skull, jaws and cervical part of the spine should be undertaken as a routine.

##### Treatment.

In the early stages of the neuralgia it is usual for the bouts to subside in the course of a few days or weeks, after which the patient may be quite free from pain for months or even years. Sedatives and analgesics may help to tide him over the attacks. Numerous drugs have been advocated, but none has stood the test of time. Sooner or later the severity and frequency of occurrence of the attacks increase to an intolerable degree, and surgical measures are required. Such measures should not be delayed unduly, as they usually give dramatic relief of pain, and even when there are undesirable complications the patient is most grateful. To advise against surgical treatment and thus condemn a patient to a life of pain and despair, on the grounds that the treatment is worse than the disease, is indefensible. Such advice, however, is occasionally given by doctors.

##### Injectations.

Injectations of alcohol into a sensory nerve serve to put it out of action for some months, after which recovery occurs. The area of skin or mucous membrane innervated by the nerve is rendered insensitive. When the injection is made into the Gasserian ganglion some cells may be destroyed, so that their fibres will not regenerate. The effect of such an injection may be of long duration or even permanent. It should be the aim of the surgeon to limit the destruction of nerve tissue to the least that will serve to relieve pain. In practice it is sufficient in the early stages to render the region of the trigger point insensitive. When it is in the field of the infraorbital nerve the latter is injected at the infraorbital foramen. This entails practically no risk and but little subsequent disability, whilst the results are good, pain being relieved for a period of from six months to a year or two. The injection may be repeated several times as may be necessary. Eventually it may fail, and other procedures will have to be considered. When the trigger point is in the lower lip, lower gum or tongue, the injection is made into the third division of the fifth nerve at the *foramen ovale*. Here there is not much risk of serious trouble, but anaesthesia of part of the tongue and mouth is a source of trial to the patient.

When the injections mentioned above fail to give relief, or when the neuralgia involves two or more divisions of the fifth nerve, injections into the Gasserian ganglion are sometimes made. The risks in this case are much greater, in that it is difficult to control the amount of destruction of the ganglion; and if the cornea is rendered insensitive, keratitis may occur. Unskilful injections may lead to other troubles as well. In favourable cases, however, prolonged or even permanent relief may be achieved.

##### Operations.

Nowadays operations upon the peripheral branches of the fifth nerve are seldom performed. If injections fail, or are not considered advisable, it is usual to divide the sensory root of the nerve, either completely or in part. There is no regeneration after division of the fibres in the root, so that results achieved are permanent. Division of that part of the root concerned in the innervation of the region in which the trigger point is situated and pain is felt is ideal and should be attempted. The chief objection to this is that sometimes the pain crops up in the area which has not been rendered insensitive.

It is important to leave intact the sensation of the cornea, but when the neuralgia involves the upper part of the face this sensation may have to be sacrificed. The motor root should not be damaged.

Most neurosurgeons use the subtemporal, extradural approach to the sensory root, but Dandy claimed certain advantages for his "cerebellar" approach.

Division of the descending tract of the fifth nerve in the *medulla oblongata* would seem at first sight to offer great advantages, in that much of the sensation of the face is left undisturbed whilst pain sensation is eliminated, but the risks involved are sufficient to rule it out except in special circumstances.

The operation of decompression first advocated in 1952 by Taarnhoj has given encouraging results, although sufficient time has not yet elapsed to permit of final judgement. If the early promise is fulfilled, major injections, root sections and tractotomies will soon be forgotten. In this operation the *dura mater* over the sensory root is divided, but the nerve itself is not harmed. Thus the undesirable effects of nerve destruction are completely avoided.

If during the investigations abnormalities have been discovered, such as retained stumps of teeth, infections of nasal sinuses, intracranial tumours or aneurysms, disseminated sclerosis *et cetera*, these should receive appropriate atten-

tion; but as a rule this will not influence the course of the *tic douloureux*. Teeth should not be extracted excepting when it is necessary for adequate dental reasons.

#### Undesirable Effects of Nerve Destruction.

After destruction of the fifth nerve, either wholly or in part, and whether by alcohol injections or operation, there is loss of sensation in the affected part of the face, mouth and nose. What sensation remains is subserved by other nerves. The spasmodic pain is relieved completely. Usually the patient experiences curious creepy sensations referred to the desensitized region, which may be an annoyance. Occasionally there is a burning, persistent pain, which may mar seriously the result of treatment. When the cornea has been rendered insensitive, it may subsequently become inflamed and ulcerated. These are the most important of the undesirable effects of destroying the sensory nerve of the face, but at worst the price of relief is justifiable. If it proves to be possible to alleviate pain without damaging the fifth nerve, as in the operation of decompression, a great advance will have been made.

HUGH C. TRUMBLE,  
Melbourne.

## British Medical Association News.

### ANNUAL MEETING.

THE annual meeting of the Tasmanian Branch of the British Medical Association was held at the Royal Society's Rooms, the Museum, Hobart, on February 13, 1954. Dr. A. PRYDE, the President, in the chair.

#### ANNUAL REPORT OF THE COUNCIL.

The annual report of the Council, which had been circulated among members, was taken as read, received and adopted on the motion of Dr. A. Pryde, seconded by Dr. H. M. Fisher. The report is as follows.

The Council of the Tasmanian Branch presents the report for the year ending December 31, 1953.

#### Membership.

The present membership of the Branch is 222, including one life member and two complimentary members. This compares with the membership of 208 at the last annual meeting, indicating a gain of 14 members. During the year nine new members were elected and fourteen transferred from other States. The losses were nine, made up by five transfers to other States, two deceased, one expelled and one resigned.

#### Obituary.

During the year the following deaths occurred, which we record with regret and sympathy to the families: Dr. Stuart Gibson, a former President of the Branch, and Dr. E. M. Allester, of Huonville.

#### Meetings.

There were no general meetings of the Branch held this year apart from the annual meeting, the business of the Branch being considered at the meetings of the Northern and Southern Divisions as indicated in their annual reports.

#### Council.

Fourteen meetings of the Branch Council were held during the year, including two special meetings. Record of attendance was as follows:

	Meetings.
Dr. A. Pryde (President) . . . . .	11
Dr. A. O. Green (Vice-President) . . . . .	9
Dr. B. Hillier (Treasurer) . . . . .	12
Dr. T. Giblin (Federal Council Representative) . . . . .	12
Dr. J. B. G. Muir (President-Elect and Federal Council Representative) . . . . .	10
Dr. Franklin R. Fay (Honorary Medical Secretary) . . . . .	14
Dr. C. W. Clarke (Honorary Secretary, Southern Division) . . . . .	7
Dr. R. A. Godfrey-Smith (Honorary Secretary, Northern Division) . . . . .	12
Dr. P. Braithwaite (Councillor) . . . . .	9
Dr. A. Millar (Councillor) . . . . .	12
Dr. D. Waterworth (Councillor) . . . . .	9
Dr. R. A. Lewis . . . . .	2
Dr. G. M. W. Clemons . . . . .	1

<sup>1</sup>Members of last year's Branch Council, which held two meetings in the period under review.

### Representation.

The Branch has been ably represented on Federal Council in the past year by Dr. T. Giblin and Dr. J. B. G. Muir. It is with regret that we no longer are represented by Dr. T. Giblin, who did not accept nomination for the next year. The Council wishes to record its appreciation of the time and energy expended by Dr. Giblin on our behalf over the last seven and a half years that he has been on the Federal Council.

For the coming year the Council has elected Dr. J. B. G. Muir and Dr. L. N. Gollan as Branch representatives at Federal Council. During the past year the following members represented the Branch on other bodies:

*Australasian Medical Publishing Company, Limited:* Dr. W. L. Crowther.

*Road Safety Council of Tasmania:* Dr. F. Phillips.

*Federal War Relief Fund (1939 War):* Dr. Godfrey-Smith, Dr. Giblin, Dr. Franklin Fay.

*Medical Officers Relief Fund (Federal):* Dr. Hillier, Dr. Gibson, Dr. F. W. Fay.

*Tasmanian Physiotherapy Board:* Dr. A. McL. Millar.

*Tasmanian Post-Graduate Committee in Medicine:* Dr. J. B. G. Muir.

*Tasmanian Health Education Council:* Dr. G. Robbie.

*Committee of Inquiry Under National Health Act:* Dr. Whishaw, Dr. Giblin, Dr. A. Young, Dr. L. N. Gollan.

### Ethics Committee.

The Ethics Committee this year consisted of Dr. Giblin (Chairman), Dr. Pryde, Dr. Muir, Dr. A. Millar, Dr. Godfrey-Smith and Dr. F. R. Fay (Secretary). One meeting was held for the election of Chairman and Secretary; no other meeting was called during the period under review.

### Newsletter Committee.

Dr. P. Braithwaite, Dr. C. Clarke and the Medical Secretary comprised the Newsletter Committee. There were five Newsletters published during the year. An innovation, namely, the introduction of an "Unofficial" section to the Newsletter, was commenced and appeared to be favourably received by most members.

### Publicity Committee.

Dr. Pryde, Dr. Green, Dr. Fay and Dr. Godfrey-Smith were members of the Publicity Subcommittee. Fortunately it was necessary only on two or three occasions for statements to be made in the Press, the usual need being to enlighten the public after the appearance in the Press of an ambiguous or ill-informed public statement which reflected on the Association.

### Workers' Compensation Committee.

Dr. Waterworth, Dr. Green and Dr. A. Millar represented the Branch in negotiations with the underwriters. The schedule agreed upon last year is generally satisfactory, but no provision for specialist consultations is made, so further negotiations are being undertaken.

### Medical Fees Committee.

The personnel of the committee were Dr. Pryde, Dr. Gollan, Dr. Godfrey-Smith, Dr. Clarke, Dr. Franklin Fay, Dr. Butler and Dr. Gibson. No meetings were held in the period under review.

### Rules Committee.

Dr. Braithwaite, Dr. A. Millar and Dr. Franklin Fay undertook the preparation of a new and revised Branch rule book of which you have now received copies and which is to be submitted for approval at this annual meeting. The committee met on three occasions and then submitted a draft of the proposed rules to the Branch Council.

### Coronial Inquiries.

Following the request of southern members that the Attorney-General be approached to modify the *Coroner's Act* to ensure that medical practitioners should not be victimized by a disgruntled relative of a deceased patient, Dr. Giblin, Dr. Green and Dr. F. R. Fay had an interview with the Attorney-General. The Council was assured by the Attorney-General that no victimization would occur, and the Council's representatives were reassured that the *Coroner's Act* was quite satisfactory as it stood, and political pressure had no place at all in influencing a decision to hold an inquiry under the Act.

### Repatriation.

Following complaints from the Deputy Director of Repatriation in Hobart that the department was receiving an excessive number of accounts for week-end emergency treatment of repatriation patients whose local medical officers were not available, it was decided after consultations with the Divisions that any doctor visiting a repatriation patient for an accepted disability in the absence of the local medical officer during a week-end would render his full account to the patient's local medical officer, who should pay it and collect the usual repatriation fee for a visit from the department.

### Wages Board.

The Branch was represented on the Doctors Wages Board, formed to determine the wages of receptionists in doctors' surgeries, by Dr. Dorney and Dr. Clemons. Following several meetings of the Board, the scale of wages was fixed, based on a forty-hour week. Examples are: Trained nurse, £11 4s. 3d. per week after twelve months' service. A non-trained nurse is 9s. 6d. less, and there are other classes and allowances in the scale.

### Medical Fees.

Fees for life assurances examinations: Following negotiations between Federal Council and Life Offices' Association, the fee for examination of persons for life assurance was raised to £2 2s. as from July, 1953.

Private fees: The Branch Council requested members in April to stabilize their fees, and to avoid any increase in fees following the introduction of the national health scheme. It is the policy of the Association that fees should remain at their present level and not be raised to the maximum obtainable under the national scheme.

### Pharmaceutical Benefits Act.

This aspect of the *National Health Act* continues to function satisfactorily. There have, so far, been no complaints of abuse by members of this Branch.

### Pensioner Medical Service.

This also continues to work satisfactorily—members participating receiving 9s. and 11s. respectively for a consultation or a visit. The Committee of Inquiry, the personnel of which has been mentioned, was formed during the year to investigate any alleged breaches of the Act. The Branch Council is supporting moves on a federal level to prevent an increase in the percentage of the population entitled to this concessional service consequent upon relaxation of the means test for pensioners. The Branch Council, after reference of the subject to divisions, supported the request of friendly societies that certificates to lodge members who were also pensioners should be given without extra charge.

### The National Health Act.

#### Medical Benefits.

The Branch Council has requested members to itemize their accounts and receipts correctly and thus facilitate the work of the insurance companies and to ensure maximum benefits to the patient.

The Branch Council views with concern, as does Federal Council, the high proportion of accounts which are partly settled by payment of the benefit direct to the doctor before the patient has paid his share. This matter received consideration at federal level and Sir Earle Page was requested to bring in a regulation to avoid such a procedure except in cases of financial hardship, but the request was refused.

Many anomalies have been reported by members in the Schedule of Commonwealth Benefits, and these, together with other States, have been correlated and submitted to Sir Earle Page for consideration. It is only to be expected that such "teething troubles" will mark the first few years of such a major scheme as the National Health Scheme, and your Council urges your support in honest cooperation with the Commonwealth in making this scheme a success.

### Hospital Policy.

The honorary system still persists in the metropolitan public hospitals in Tasmania, in spite of the absence of any means test. On several occasions the State Minister has been approached to pay visiting members of the staff, but his answer is always "no money to spare, although we agree you should be paid". The Council supports the introduction of intermediate beds in public hospitals, but so far the State Government will not agree to it.

### Branch Rules.

Following a submission of a draft of the new and revised Branch rules by the Rules Committee, the Branch Council held a special meeting to consider them in detail. Following this the draft was submitted to the Branch solicitor, Mr. H. S. Baker, who suggested several amendments, with which your Council concurred, and he expressed the opinion that the proposed rules were generally satisfactory. The amended draft was then printed and has been circularized to members. The main innovations in the proposed new book of rules are:

- (a) A preliminary section consisting of relevant extracts from the Memorandum, Articles and By-Laws of the British Medical Association.
- (b) Changes in Branch Council Constitution, namely:
  - (i) The retention of the President for an extra year as Past President.
  - (ii) All elections to be by postal voting, and counting to be on a preferential system.
  - (iii) Ordinary members of Council to be elected by Divisions, each Division being entitled to one councillor for every 50 members.
- (c) A greatly increased ethical section bringing our Branch rules into line with the majority of other States.
- (d) A final section with relevant extracts from the Articles and By-Laws of Federal Council.
- (e) An index.

These rules are to be submitted at the annual meeting for approval by members of the Branch. If passed, they will have to be approved by the Council of the British Medical Association in England before they come into force.

### Reports of Divisions.

The annual reports of the Divisions to Branch Council are as follows:

#### Southern Division.

*Annual General Meeting*.—Tuesday, February 24, 1954. The following office-bearers were elected: Chairman, Dr. P. Braithwaite; Vice-Chairman, Dr. A. L. Stephenson; Honorary Treasurer, Dr. J. M. Gunson; Honorary Secretary, Dr. Colin Clarke; Executive Committee, Dr. R. J. Hudson, Dr. John Dobson, Dr. K. J. Friend.

Meetings were held: March 26, 1953; April 22, 1953; April 29, 1953 (address, Mr. McNary, "Medical Benefits"); August 19, 1953; September 30, 1953 (address, Dr. Phillips, "Royal Tragedies").

The last meeting of the year has been arranged for Tuesday, January 12, 1954. Four executive meetings were held during the year.

(Signed) COLIN CLARKE,  
Honorary Secretary.

#### Northern Division.

*Office-Bearers and Membership*.—The following office-bearers were elected for 1953: Chairman, Dr. L. N. Gollan; Vice-Chairman, Dr. M. W. Fletcher; Honorary Treasurer, Dr. L. H. Wilson; Honorary Secretary, Dr. R. A. Godfrey-Smith; Members of Executive Committee, Dr. D. B. Nathan, Dr. H. J. C. English, Dr. R. Wall.

The number of members of the Division at the beginning of the year was 82, and at the end of the year 85.

Meetings: Eleven general meetings were held during the year, including the annual meeting and one special general meeting. The average attendance at meetings was 28. The special general meeting was held on February 23 to hear a lecture by Sir Allen Daley, formerly Chief Health Officer to the London County Council. The lecture was entitled "London during the Blitz".

At a monthly general meeting held on Thursday, April 30, Mr. W. S. McNary, an executive of an American medical insurance society, addressed the Division on "Medical Benefits Plans in America and Australia".

Five members of the Division addressed monthly general meetings on medical subjects:

On April 2, Dr. S. M. Bates: "The Modern Treatment of Otitis Media."

On June 4, Dr. L. N. Gollan: "The Use of Butazolidin in Arthritis: A Preliminary Report."

On July 2, Dr. H. M. Fisher and Dr. G. D. Cribb: "The Early Diagnosis of Cancer: Some Conclusions at the

End of the First Twelve Months' Work at the Hallstrom Clinic, Launceston."

On August 6, Dr. J. L. Grove: "Radio-Active Iodine in the Investigation and Treatment of Thyroid Disease."

At the monthly general meetings held in March, April and October, cases or records of cases and commentaries were presented by Dr. Stevens, Dr. Gollan, Dr. Fletcher, Dr. Gunson, Dr. Ingram, Dr. O'Brien, Dr. Wilson and Dr. Godfrey-Smith.

Four films were shown at meetings: On September 3, "Intussusception" and "Care of the Premature Baby". On December 10, "The Nature of Tuberculosis" and "Let's Keep Our Teeth".

The successful repetition of a monthly general meeting held at the Devon Hospital, Launceston, was especially gratifying to the executive. This meeting had the highest attendance (37) of all the monthly general meetings held throughout the year, and the number included many members from the north-west coast. It is hoped that such a meeting will become a regular annual event.

**Annual Post-Graduate Week-End Course and Dinner.**—The twenty-seventh annual post-graduate week-end course was held at the Launceston General Hospital from Friday, November 20, to Sunday, November 22. Visiting lecturers were Professor B. T. Mayes and Dr. T. M. Greenaway, both from Sydney. Each gave a clinical demonstration and three lectures: Professor Mayes: "Prolonged Labour"; "Obstetrical Emergencies: (a) Traumatic Post-Partum Haemorrhage, (b) Constriction Ring, (c) Bleeding at Caesarean Section, (d) Prolapsed Cord"; "The Pregnant Diabetic". Dr. Greenaway: "Anaemia"; "Functional Disorders in General Practice"; "Thyrototoxicosis".

Sixty-three members and visitors attended the course, and forty-nine attended the annual dinner which was held at Overton House on Saturday, November 21. Both functions were very successful from all points of view, and the Executive Committee was well satisfied that the usual high standard of the course and dinner had been maintained if not improved upon.

**Obstetrical and Gynaecological Section.**—At the annual meeting of the section held on January 29, Dr. Fisher was elected Chairman and Dr. Thomson, Secretary. Besides the annual meeting five other meetings were held, and at each of these lectures were given or cases discussed.

The Board of the Queen Victoria Hospital now consists of seven members, four of whom are government nominees, and three are elected by the Queen Victoria Association. At the suggestion of the Minister for Health the medical staff committee, which meets on the same night as the Obstetrical and Gynaecological Section, has been formed into a medical advisory committee to the Queen Victoria Hospital Board.

**Library Committee: Sir John Ramsay Memorial Library.**—During the year the library was transferred from the basement of the main building of the Launceston General Hospital to its new quarters near the Pathology Department. Owing to this change, the library facilities were very limited for several months, but the journal section is now in fairly good order, and it is hoped to complete the arrangement of the book section in the coming year. The inconvenience caused by the change is regretted, but members will appreciate the greatly increased convenience and comfort of the new library, as well as its more pleasant surroundings.

It is hoped that some new books can be added to the library during the year, and suggestions from members will be welcomed.

The Library Committee, consisting of Dr. Grove, Dr. Wall and Dr. Hogg, met on several occasions to consider library matters and finance.

**Payment of Part-Time Specialists in Government Hospitals.**—This matter, which was the subject of so much discussion and negotiation in 1952, has remained quiescent throughout most of the year. Following a recommendation from this Division, the Branch Council again took the matter up with the State Minister in July, with no result except a rather non-committal letter from him expressing his hopes for the future. It appears that no early change can be expected in the present unsatisfactory state of affairs.

**National Health Bill.**—Details of the bill were discussed on several occasions at general meetings, and a number of suggestions for improvement have been recommended to Branch Council. It is understood that many recommendations from all Branches will be considered by Federal Council at its next meeting, and may become the subject of negotiation with the Federal Minister in due course.

**Federal Council.**—For several years no member of this Division has served on the Federal Council, and as a result our members have sometimes felt out of touch with Federal Council thought and action. Therefore when Dr. Clemons attended the February meeting of Federal Council as substitute for Dr. Giblin, the division warmly welcomed the outline of proceedings that he was able to give a subsequent general meeting. The Division is pleased to learn that one of its members has been elected by Branch Council as Federal Councillor for 1954, and congratulates Dr. Gollan on his appointment.

**Medical Benefits Fund of Australia.**—A few teething troubles have been experienced in the operation of this and other health insurance schemes, but generally they appear to be working very well. The chief difficulty appears to have been in getting practitioners to refer to the date and nature (or schedule number) of each service in their account forms.

**Publicity.**—At the beginning of the year the Branch Council appointed a Publicity Subcommittee of four members, two each from the Northern and Southern Divisions. Each pair of members was given authority to act independently within its own sphere, with a view to having publicity matters dealt with promptly. This arrangement has worked very well in the north, and on several occasions where matters calling for correction or comment have appeared in the lay Press, a statement attributed to "a spokesman for the B.M.A." has been published in the next issue.

**Wages Board for Employees at Doctors' Surgeries.**—Dr. Clemons was appointed as one of the representatives for the employers, and a subcommittee consisting of the Chairman, Dr. Clemons, Dr. Grove and Dr. Stevens and the Honorary Secretary met on three occasions to discuss the case to be put before the Board. It was generally felt that the profession's interests were well presented and that the outcome of negotiations was not as bad as it might have been. Many members were bewildered by the somewhat explosive haste with which the negotiations were arranged and concluded by the Department of Labour and Industry.

**Pathology Services for Private Patients in Launceston.**—Certain pathology services, notably the estimation of prothrombin time, have been unavailable to private patients in Launceston, and it was pointed out at a general meeting that this sometimes caused the withholding of desirable treatment or the otherwise unnecessary occupation of a public hospital bed. Representations to obtain the required services were made firstly to the Commonwealth Health Laboratory and later to the Board of the Launceston General Hospital, but unfortunately these were met with some long-term promises from the first organization and with refusal from the latter.

**Fees for Specialist Services in Workers' Compensation Cases.**—In most compensation cases where specialist attention is recommended by the practitioner attending, the insurance company or the employer is agreeable to paying an appropriate fee, and does so by private arrangement. However, cases have occurred in which an insurance company has agreed to the seeking of specialist advice and later refused to pay more than the scheduled fee. At the request of this Division the Branch Council is taking up the matter with the Underwriters' Association, with a view to securing the incorporation in the schedule of an appropriate fee for specialist examination and opinion.

**Branch Rules.**—The proposed Branch Rules were discussed at the December general meeting, and several small modifications were suggested. It was generally felt that the Rules Subcommittee should be congratulated on the work they have done on the proposed revision.

**Executive Committee.**—The Executive Committee met on eleven occasions throughout the year for the conduct of business. Attendances were as follows: Dr. Gollan, eight meetings; Dr. Fletcher, nine meetings; Dr. Wilson, seven meetings; Dr. Nathan, seven meetings; Dr. Wall, seven meetings; Dr. English, nine meetings; Dr. Godfrey-Smith, eleven meetings. Dr. Ramsay, Dr. Maloney and Dr. Churton, whose membership ceased after the annual meeting in February, each attended one meeting.

(Signed) R. A. GODFREY-SMITH,  
Honorary Secretary.

#### General Practitioner Group.

The end of 1953 saw the formation of a Special Group of the Tasmanian Branch of the British Medical Association, with the object of promoting the interests of the profession in all matters pertaining to general practice.

## BRITISH MEDICAL ASSOCIATION.

## TASMANIAN BRANCH.

## Income and Expenditure Account, Year Ended December 31, 1953.

EXPENDITURE.				INCOME			
	£	s.	d.		£	s.	d.
To Secretary's Salary .. .. .			303 6 8	By Members' Subscriptions .. .			1,538 3 0
" Printing, Stationery, Typing and Duplicating (Including News-letters and Draft Rules) ..	308 16 6			" Interest:			
" Postage, Duty Stamps, Telephone and Telegrams .. .	46 11 6			Debentures .. .	18 4 0		
" Rent of Room (Annual Meeting) ..	1 0 0			Commonwealth Loans .. .	35 14 0		
" Papers .. .	7 0 0			" Sales of Car Badges .. .		53 18 0	
" Travelling Expenses:			363 8 0	" Deficit .. .		221 17 2	
Branch Council .. .	75 0 0						
Secretary .. .	3 15 0						
" Legal Expenses .. .			78 15 0				
" Capitalisation Fees:			45 3 0				
Federal Council .. .	218 8 0						
Australasian Medical Publish- ing Company, Limited ..	426 6 0						
British Medical Association, London .. .	275 11 0						
Southern Division .. .	56 0 0						
Northern Division .. .	43 0 0						
" Audit Fee .. .	6 6 0						
" Code Address .. .	3 3 0						
" Bank Charges .. .	1 18 1						
			11 7 1				
			<u>£1,821 4 9</u>				<u>£1,821 4 9</u>

## Headquarters Fund Account, 1953.

	£	s.	d.		£	s.	d.
To Balance, January 1, 1953 .. .			217 0 8	By Balance, December 31, 1953 .. .			222 9 8
" Bank Interest .. .			5 9 0				
			<u>£222 9 8</u>				<u>£222 9 8</u>

## Balance Sheet as at December 31, 1953.

LIABILITIES.				ASSETS.			
	£	s.	d.		£	s.	d.
Capital Account:				English, Scottish and Australian Bank, Limited ..	68 3 6		
Balance, 1952 .. .	2,204 0 11			Commonwealth Treasury Bonds (£1,360) .. .	1,327 5 0		
Australasian Medical Publishing Company, Limited—Deben- tures .. .	159 15 0			Australasian Medical Publishing Company, Limited—Deben- tures .. .	586 1 3		
	<u>2,363 15 11</u>			War Savings Certificates .. .	133 0 0		
Less Deficit for year .. .	221 17 2			Furniture—Cupboards .. .	30 0 0		
War Relief Contributions .. .			2,141 18 9				
			<u>2 11 0</u>				
			<u>£2,144 9 9</u>				<u>£2,144 9 9</u>

Audited and found correct.

(Signed) ADAMS AND BENNETTO.

Chartered Accountants (Aust.).

The acting office-bearers are: Chairman, Dr. T. James; Vice-Chairman, Dr. H. B. Roberts; Secretary-Treasurer, Dr. R. J. Turnbull. The inaugural meeting has not yet been held.

## Branch Dinner.

Following the annual meeting last year the British Medical Association dinner was held at St. Ives Hotel in Hobart. Dr. Mervyn Archdall was our guest. There were 35 members present, and in view of the number of members in practice in Hobart it was felt that the attendance was rather on the low side. In view of this a slightly less elaborate dinner at Wrest Point is to be held this year, and it is hoped that many more will attend and join in the convivial gathering of their colleagues.

## Conclusion.

As this report indicates, there has been quite a lot of work done by your Branch Council during the year.

Provided the new rules are approved, the Council will in the future be slightly larger and there will be better representation of the Northern Division. It is hoped that this will eliminate any feeling of being neglected which the northern members may have had. It is noted that the Northern Division far outshines the Southern Division in clinical meetings and catering for the medical side of the British Medical Association activities. It is the Council's hope that the new executive of the Southern Division will be able to infuse more life into this aspect of the British Medical Association in southern Tasmania.

Finally, as we start our new year on the eve of a visit by Her Majesty Queen Elizabeth and the Duke of Edinburgh, who is an honorary member of the Association, the Council feels that it is appropriate that we as a Branch should here reaffirm our loyalty to the Throne.

(Signed) A. PRYDE,  
President.

#### FINANCIAL STATEMENT.

The financial statement for the year 1953 was presented by the Honorary Treasurer, Dr. Berthold Hiller. He explained that the deficit was largely due to expenses incurred in the compilation of the new rules. The statement was adopted on the motion of Dr. Hiller, seconded by Dr. J. Bruce Hamilton. The statement is published herewith.

#### DRAFT RULES.

The President moved that the new draft rules which had been submitted to members should be adopted. The motion was seconded by Dr. F. R. Fay and carried.

#### ELECTION OF OFFICE-BEARERS.

The President announced that the following had been elected office-bearers for the year 1954:

President: Dr. J. B. G. Muir.

President-Elect: Dr. W. K. McIntyre.

Vice-President: Dr. T. Giblin.

Honorary Treasurer: Dr. B. Hiller.

Honorary Secretary: Dr. F. R. Fay.

Members of Council: Dr. P. Braithwaite, Dr. K. Friend, Dr. W. M. Fletcher.

Messrs. Adams and Bennetto were elected auditors for 1954.

#### INDUCTION OF PRESIDENT.

Dr. A. Pryde introduced the President for 1954, Dr. J. B. G. Muir, and vacated the chair in his favour. Dr. Muir thanked the members for his election.

#### RETIRING PRESIDENT'S ADDRESS.

The Retiring President, Dr. A. Pryde, delivered an address on the history of the British Medical Association in Tasmania. The address has not been submitted for publication.

### Medical Societies.

#### PÆDIATRIC SOCIETY OF VICTORIA.

A MEETING of the Pædiatric Society of Victoria was held at the Royal Children's Hospital, Melbourne, on Wednesday, February 10, 1954. The meeting took the form of a series of papers on infantile diarrhoea.

#### The Serological Diagnosis of Salmonella and Shigella Infection in Infants and Children.

MISS FREDA FRIDAY presented the results of work done in the pathology department of the Royal Children's Hospital on the serological diagnosis of salmonella and shigella infection in infants and children. The report will be published in detail at a later date. Briefly, Miss Friday said that 96 patients between the ages of three days and thirteen years with a clinical diagnosis of enterocolitis had been investigated by cultural and serological methods for infection with strains of salmonella and shigella. Those organisms were isolated from stools or rectal swabs of 42 patients, and the serological findings were sufficiently characteristic and specific to warrant the following conclusions: An appropriate salmonella "O" agglutinin titre of 1:10 and an "H" titre of 1:40 or greater at the time of the patient's discharge from hospital was reasonably diagnostic of *S. typhimurium* infection, and this finding was probably applicable to all pathogenic strains of salmonella. A specific agglutinin titre of 1:20 or greater at any time during the illness was diagnostic of *Sh. flexneri* infection at the Royal Children's Hospital.

Application of these conclusions to the culturally negative group raised the incidence of infection with salmonella or shigella from 43.5% to 55.5% in the entire group, and from 48% to 62.6% in the over four months age group.

No diagnosis of infection was made on serological grounds alone in infants under four months of age, but the isolation

of *S. typhimurium* from six children in this age group was associated with a significant serological response in five instances. The youngest of these infants had agglutinin titres of 1:640 to 1:0 and 1:5 respectively at the age of nine weeks.

Miss Friday emphasized the responsibility of both paediatrician and bacteriologist in completely eliminating the group of patients still discharged from hospital with a diagnosis of enteritis of unknown aetiology.

DR. J. W. PERRY, in opening the discussion, acknowledged the help given to Miss Friday by the medical and laboratory staffs of the hospital, and by the staff of the Public Health Laboratory. He said that the results which had been obtained by a combination of bacteriology and serology had raised significantly the number of positive diagnoses. Blood should be taken for serological examination from all patients in the diarrhoea ward. As infants less than four months old had a poor serological response, attention must be concentrated on more complete identification from faecal cultures. Dr. Perry mentioned that since Miss Friday had been carrying out her investigation pathogens had been grown from 43% of 96 patients. During the previous four years pathogens had been grown from only 28% of 947 patients. That indicated that more careful culture techniques could have been responsible, and the figure of 28% might have been raised if improved technique, with the addition of brilliant green to the culture medium, had been used.

DR. ROSE MUSHIN said that the number of positive results was impressive. The figure of 28% for positive results from cultures over the previous four years quoted by Dr. Perry was probably less when one considered that a few years previously the incidence of cross infection in the hospital was higher. Dr. Mushin then asked three questions: Were any of the infections in Miss Friday's series of patients cross infections, or were all of them sporadic? Were the results based on more than one stool culture? How many patients in the series were in the age group two to fourteen years? Dr. Mushin said that in that group the percentage isolation of organisms was much higher.

Miss Freda Friday, in reply to Dr. Mushin, said that the laboratory workers were concerned only with the diagnosis of enteritis, and she did not know how many of the patients had cross infection. For every patient at least three stools were submitted to culture. Most patients were less than two years of age. The average age of those with salmonella infection was seven months, only two being older than one year, and the average age of those infected with shigella was five months, three being older than one year.

DR. MICHAEL WILSON, from the Public Health Laboratory, said that the Royal Children's Hospital was the chief source of stools which grew salmonella organisms. If practitioners sent in more specimens to the Public Health Laboratory, a more complete picture of the incidence of salmonella infection in the community would be obtained. Dr. Wilson said that there was much salmonella at large in Melbourne. The identification of pathogens could be improved serologically, by including a wider range of antigens, but practical considerations precluded that at present. Undoubtedly there were numerous unclassified organisms responsible for infective diarrhoea. The serologist found only what he was looking for. *Salmonella seftenberg* was one of the commonest of the group. It had turned up first in Melbourne in 1950, and every stool from which the organism had been grown had come from the Royal Children's Hospital, until the recent typhoid epidemic. When workers at the Public Health Laboratory had commenced searching for *S. typhosus*, they discovered *S. seftenberg* consistently in one particular brand of coconut.

DR. E. V. KEOGH said that in many instances infective diarrhoea was due to unidentified pathogenic agents. There existed a tendency to take laboratory results too literally, and to assume that, as no recognized pathogen had been isolated, the disease was due to a non-infective cause. By use of improved cultural and serological techniques, it should be possible to identify the causal organism more frequently, a decreasing percentage of instances being left in which a causative organism was not isolated. The problem was more difficult in infants less than four months of age, in whom a mild infection might not produce antibodies. In that age group, there would probably be a higher incidence of non-infective diarrhoea. The most common pathogen in infants from four to twelve months old was salmonella, and in infants older than one year shigella was found more frequently. Experience during the last world war had been that if shigella was not cultured from diarrhoeal stools early in the illness, there was great difficulty in culturing it at all. This was in contrast to salmonella infections, in which a stay in hospital improved the chances

of a positive result. There was very little evidence that *E. coli* or viruses were responsible for much diarrhoea at the Royal Children's Hospital.

Dr. D. B. PITT asked what role *Staphylococcus aureus* played as a cause of infective diarrhoea in infancy.

Dr. J. W. PERRY, in reply to Dr. Pitt, said that his own experience with *Staphylococcus aureus* in its relation to diarrhoea was limited, but competent bacteriologists considered that it was pathogenic in various age groups. Dr. Perry said that his experience was confined to sporadic cases. Until recently, bacteriologists at the Royal Children's Hospital had not been searching for the organism, but over the past few months, *Staphylococcus aureus* had been grown from the stools of four infants. Dr. Perry quoted the case of an infant who had died, and at whose post-mortem examination extremely severe enteritis was found. A pure culture of *Staphylococcus aureus* was grown from the Peyer's patches.

Dr. H. McLOKININ asked if the serological investigation carried out by Miss Friday had any application to public health work. He quoted an example in which an outbreak of diarrhoea had occurred at a nearby holiday resort each year for several years, and appeared to originate from the same source. Could serology aid in the identification of that source?

Dr. J. W. PERRY, in reply, said that serological identification was more difficult in adults in whom a miscellaneous collection of antibodies was commonly found. Also, antibodies from T.A.B. immunization produced confusion.

#### A Social Survey of Infective Diarrhoea in Infancy, with its Distribution, in Melbourne and Suburbs, 1952-1953.

MISS JEAN ALLAN, S.R.N., Dip. Soc. Studies, said that fifty years previously infective diarrhoea had been listed under preventable diseases as the main cause of infantile deaths in Australia. At that time, it accounted for 25% of all deaths in children under twelve months of age in Victoria. The introduction of municipal sanitation, the substitution of garages for stables during the first decade of the century, and the educational campaign in favour of breast-feeding and improved infant hygiene pursued by the Infant Welfare Centres since 1917, had resulted in infective diarrhoea accounting for only 5% of all infantile deaths in Victoria by the end of the second World War. In the past five years there had been a further noticeable decrease, and in 1952 slightly more than 1% of all infant deaths had been due to the disease.

While the mortality rate of infants suffering from infective diarrhoea had fallen in Victoria since the last war, the disease itself was still a major problem at the Royal Children's Hospital, and records indicated that the incidence of the disease was increasing. During the war years an average of 240 children had been admitted each year with a diarrhoeal disease—one in every 86 babies born. During the past three years more than 400 children had been admitted to hospital each year—an average of one in every 62 babies born. Many more had been treated as out-patients. The number of hospital admissions of patients, either as in-patients or as out-patients, represented only a fraction of the total number of cases encountered in the community. Late in 1952 diarrhoea of more than forty-eight hours' duration became a notifiable disease in Victoria; but until figures were available, it was impossible to know how many additional patients had been met with and treated in general medical practice.

With the knowledge that children were being admitted to hospital in numbers out of proportion to Melbourne's rapid post-war increase in population, the Clinical Research Unit at the Royal Children's Hospital had commenced a study of the social backgrounds of those children in an endeavour to find out what social factors, if any, influenced the cause and spread of infective diarrhoea and what steps might be taken to prevent some of the infections.

Between February, 1952, and May, 1953, a study was made of 174 children under the age of two years who had been admitted to the hospital with infective diarrhoea. The children studied were those admitted directly from their own homes, all of which were in the greater Melbourne area, roughly within a twenty-mile radius of the hospital. Excluded from the survey were those babies transferred from other wards of the hospital, or admitted from other hospitals (mostly maternity hospitals), babies' homes or children's institutions, and those who came from outside the metropolitan area. It was felt that this selection of patients would give a good indication of any outstanding social factor which had bearing on the disease, since the Royal Children's Hospital admitted patients suffering from

diarrhoeal diseases without regard to locality or income group. Private hospitals did not admit such patients, and the other public hospitals providing beds for them took, by comparison, a relatively very small number each year. Miss Allan said that in order to draw any positive conclusions from such a study, a similar study would be made of a control group. That was started, but because of certain difficulties within the hospital in getting sufficient cases in the same age group and some lack of cooperation from the mothers of the children chosen as controls, the study of a control group was discontinued.

The method of carrying out the study was to arrange to visit the home of each baby within the first few days after admission. In talking to the mother the emphasis was on the baby, his present illness, the circumstances leading up to it, and the possibility of contacts or known cases of diarrhoea in the neighbourhood. Information was sought regarding pre-natal care, post-natal health, feeding, sleeping and evacuation habits, and the regularity of attendances at infant welfare centres. The source of milk supplies, time and mode of delivery, storage facilities and method of sterilization were also examined. Most of the mothers showed a considerable degree of anxiety regarding their babies, and many of them, particularly those with the cleanest homes and a good standard of personal hygiene, felt that they were largely to blame for the illnesses. It helped them all to discuss the expected course of the baby's illness and the form of treatment which was being used at the hospital. In addition, an offer of help and guidance in the post-discharge convalescent period usually helped the mothers to adopt a calmer outlook and to retain confidence in their own ability to care adequately for their babies on discharge from hospital. It was inevitable that discussions with the mothers along those lines led to more general matters and to obtaining other data which were required, such as information about other members of the household, the parents, children, relatives or others, their occupations, health and income, the children's schools and similar facts. Information regarding the dwelling, especially in relation to the size, ventilation and cleanliness of bedrooms and kitchen, facilities for storage of foodstuffs and disposal of wastes, and the adequacy and cleanliness of essential services, such as bathroom, laundry and toilet, was also recorded.

The 174 babies considered in the study remained in hospital for a period ranging from three days to five months. The average stay was fifteen days. At the time of discharge from hospital the mother was given written feeding instructions by the ward sister and referred back to her nearest infant welfare centre for future care. An appointment was also made for the baby to be examined at a follow-up clinic at the hospital a week to ten days after discharge from hospital, and during that period at least one visit was made to see the baby at home and record its progress. About a third were seen at home more than once. They were mostly babies discharged earlier than usual during periods of pressure for beds, or babies whose mothers lacked their former confidence and needed support and encouragement. Very few patients were followed up for a period extending longer than a couple of weeks. That did occur when there was some major social problem in the home, and such families were frequently referred for aid to an appropriate outside agency, such as the Victorian Society for Prevention of Cruelty to Children, the Red Cross Society, the Ladies' Benevolent Society or the Children's Welfare Department.

At the conclusion of the study a number of factors were found to stand out as probably having a considerable bearing on the incidence of infective diarrhoea. First was the seasonal and geographic distribution. The disease appeared to be endemic throughout the year, but there was a definite rise in admissions to hospital during the summer months, December to April.

The industrial areas provided cases fairly constantly throughout the year, but the incidence in other districts appeared to be mildly epidemic; for example, at one period the majority of cases would come from, say, the Footscray-Essendon-Braybrook area. A few weeks later the majority would be concentrated in suburbs as far distant as Moorabbin, Chelsea and Carrum.

On the whole there were three clearly defined areas from which infected babies were mainly admitted: (a) The thickly populated industrial areas (Richmond, Abbotsford, Hawthorn, South Melbourne, North Melbourne, Carlton, Fitzroy, Collingwood and Footscray), which produced slightly more than 40% of the total cases. (b) The new housing areas, which produced about 22% of the total cases. (c) The emergency housing areas of Camp Pell, Watsonia and Lorimer Street,

Port Melbourne, which produced about 20% of the total cases.

Of those babies admitted from the industrial areas by far the greatest number (over 80%) came from poor to sub-standard homes. In the survey a standard home was regarded as one providing lighting, a water supply to the kitchen, bathroom facilities, with the opportunity to heat water for baths, laundry facilities and satisfactory disposal of excreta. Of the homes in the industrial areas 32% were actually condemned homes within a mile of the city area. Perhaps that was to be expected when it was realized that 7500 of the 9000 homes which had been condemned sixteen years previously and listed for consideration in the original slum reclamation schemes of the Victorian State Housing Commission were still standing and occupied. Those homes frequently had no laundry or bathroom facilities, and the only water supply to the house was a tap over a gully trap in the yard. Many were in very bad repair, with leaking roofs, crumbling walls, faulty electrical wiring and leaking or non-functioning toilet systems. Some had no lighting. The rentals in a number of cases were fixed at as low as six shillings to ten shillings per week.

Most of the babies of European migrant families came from the industrial suburbs. The number was small, but nevertheless slightly higher than the proportion of migrant families in the community. However, as the European migrant tended to settle in the suburbs of Carlton, Fitzroy, Collingwood and North Melbourne, those babies would have been exposed to infection more constantly than had they lived in less crowded areas.

It was notable that, though families lived in substandard homes, often the standard of household and personal hygiene was very good. More than half the babies admitted from all areas came from clean homes, and the proportion was no lower in the industrial areas. However, despite good standards of hygiene in other respects, mothers frequently handled infants' napkins carelessly. The laundry trough, sometimes found in the kitchen, particularly in the older suburbs, was still the favourite receptacle for receiving soiled napkins, and there they remained often uncovered between the daily washes. Some mothers had the attitude that babies' excreta were harmless. It was not difficult to visualize the chain of infection, especially in fly-infested homes, and in new areas where drainage was poor. Napkins were washed in non-boiling washing machines in 15% of homes, and mothers usually used cold or warm water only in the machines. Only 40% of mothers boiled napkins regularly. Less than 3% used commercial laundries.

The second group consisted of babies who came from homes built in the post-war years and who formed about 22% of the whole. The homes included those in the new Housing Commission areas of West Heidelberg, Braybrook, Maldstone, Coburg and West Brunswick, Jordanville, Moorabbin, Highett, Springvale, Dandenong and North Melbourne, and a slightly larger number of houses which were privately built in the newer outer areas of Balwyn, Mitcham, Box Hill, McLeod, East Malvern, Burwood, Springvale, Hampton, Moorabbin, Mordialloc, Seaford, Spotswood, Kellor, Greenvale and North Coburg. Most of the families living in those homes maintained superior standards of personal and household hygiene. The income level was high enough to exclude a considerable number from attending the out-patient clinics. However, over 60% of these post-war houses were unsewered. Many were reached by unmade roads, and frequently kitchen and laundry waste was piped to the roadway, where it lay in large stagnant pools. Some Housing Commission homes had been built on reclaimed swamp land, and a number of houses visited, though not two years old, showed extensive damp marks on the walls and ceilings.

The existing sewerage system was originally designed in 1892 for a population of one million persons, at a time when Melbourne's population was still short of the half-million mark. By the beginning of the second World War Melbourne's population had reached the million, and because of a vigorous policy pursued over the years by the Metropolitan Board of Works, sewerage facilities had been provided for all areas where a reasonable degree of development had been attained. At that time only about 4% or 11,000 of the total houses in the metropolitan area, principally those in the rural area and on the sparsely settled fringe of the urban areas, were unsewered. In 1945 the position was much the same with regard to unsewered homes, but the population was increasing. Since then the position had steadily deteriorated. The development of the metropolitan area since the war had placed a great strain on the capacity of the existing sewerage system to deal with ever-increasing flows. There had been big industrial development in the post-war years, and polluted water from

manufacturing processes in addition to storm water was discharged into the sewerage system. Melbourne's population was now nearly one and a half million persons, an increase of almost half a million since the beginning of the war, and the existing sewerage system had been called on to serve a much larger number of people and to provide for areas extending far beyond the boundaries provided for in the original scheme. Much development had taken place outside areas already provided with sewerage facilities (for example, the larger Housing Commission estates), and therefore there had been a greater strain on available supplies of labour and materials than if building had been taking place within or adjacent to areas already served. In addition, fund shortages had slowed down development by the Metropolitan Board of Works in the past two years. The obvious disadvantages of the pan service, which operated in unsewered areas, had been increased by difficulties in obtaining labour because of the objectionable nature of the work. The problem of providing sufficient pans for the ever-increasing number of properties not connected to the sewerage system, and the location of new houses which rendered access over unmade roads troublesome, added to the difficulties. It was estimated at the end of 1952 that over 30,000 homes, representing 11% of greater Melbourne homes, were unsewered. From those unsewered areas, approximately one-tenth of Melbourne homes, came almost one-quarter of all the patients studied. That surely indicated that an extension of the sewerage system was a matter of considerable urgency.

The third group of patients consisted of those living in the three emergency housing areas of Camp Pell, Watsonia and Lorimer Street, Port Melbourne. The patients were mostly admitted during definite outbreaks of infective diarrhoea in the centres, and a considerable number of them had had close contact with others suffering from diarrhoea, either in their own or in the other centres, and often with families living in the industrial areas. At the time of the survey, the three centres, each of which was sewered, accommodated 4500 of the 5000 persons living in the eleven State emergency housing centres of Melbourne. The child population up to the age of sixteen years in the three centres totalled about 3000, yet they provided one-fifth of the patients studied. The infant population of Melbourne was approximately 25,000; hence the proportion of babies being admitted to hospital from the three centres was greatly in excess of those coming from the general community. Even by emergency housing centre standards, Watsonia, Lorimer Street and the Extension I Area of Camp Pell, from which came a fair proportion of cases during a Camp Pell epidemic, provided substandard accommodation. During an epidemic at Lorimer Street three coppers served 240 persons, of whom more than 100 were children under school age. At the Extension I Area of Camp Pell there was severe overcrowding in huts. Some patients came from families of which up to 11 were housed in two very small rooms, which included primitive kitchen facilities, consisting of nothing more than a stove. Water for all purposes was carried from communal laundry and bathroom blocks, which, together with communal toilet blocks, were usually in a disgustingly filthy state. Fortunately those three sections were now virtually closed. On the whole it might be said that the general standards of camp hygiene in those three centres were lower than in other centres; and there was no doubt that a very much larger percentage of patients' families living in those particular emergency housing centres maintained lower standards of personal and household cleanliness than families in the general community. The families were larger and came from a lower income group. A considerable number of fathers had been unemployed for periods varying up to eleven months. Some had joined the army after a period of unemployment, and others worked only intermittently. Several mothers were deserted or unmarried and relied on relatives for support.

Miss Allan said that the picture of patients from the emergency housing areas which she had presented might give the impression that group living in itself was a factor to be considered. It should therefore be mentioned that during the same period numerically identical groups of persons (5000 British and non-British migrants, including 2000 children) had been housed in eight similar centres controlled by Commonwealth Hostels, Limited. Those persons also lived on a community basis, with communal toilets, ablution blocks and laundries, but in addition dined in a common dining room. Meals were cooked in well-appointed hygienic kitchens and not by the tenants as in the emergency housing centres. The survey covered the period of economic recession which Australia experienced in 1952, and unemployment was marked amongst migrants living in those centres. However, unemployed people living in migrant hostels were

housed and fed irrespective of their ability to pay board. It was interesting to note that no patient was admitted from any British or non-British hostel in the metropolitan area during the period of the study.

In the group studied, about 20% more males than females were affected. That was consistent with the higher incidence of other diseases in male infants.

The distribution according to age showed that a quarter of all cases occurred in the first three months of life and half in the first six months, with a decreasing incidence in the next eighteen months. That followed the pattern reported in other places. The cases studied had been classified according to the type of infection—19 were shigella infections, 56 were salmonella infections, and 99 were classified as non-specific infections in so far as no organisms of the shigella or salmonella groups were isolated from the stool cultures.

The shigella group of 19 patients fell into an older age distribution, the youngest being two months of age. No infant was breast-fed at the time of admission to hospital, and only three were attending infant welfare centres. By far the larger number had never attended. Eight of the 19 babies came from the emergency housing areas, and the remainder from substandard homes either on the outskirts of Melbourne where there was no sewerage or in the inner industrial areas. Many knew of possible contact with other patients suffering from diarrhoea.

Hygiene in the homes was consistently poor, and they were invariably overcrowded. Four to nine children in the family was the rule rather than the exception, and incomes frequently fell below average, because of unemployment, desertion by the breadwinner or chronic illness. Miss Allan said that it was difficult to define "an adequate income", but for the purposes of the survey an average income was considered to be one ranging from the basic wage to £17 a week. Those families assessed by a means test as being ineligible to attend out-patient clinics were grouped as having incomes "above average", while those families whose weekly income fell below the basic wage, largely the unemployed, the deserted wives and unmarried mothers, and those on pensions, were considered to have inadequate incomes. Because of high rents, size of families, sheer inefficiency or other factors, possibly quite a number of the other families could very easily be classed in the last category. The working fathers ranged in their occupations from unskilled labourers to skilled tradesmen and office workers, and those in the higher income bracket included several owner-managers of businesses and those with occupations such as a company director and a chiroprapist.

The patients infected with the salmonella group were particularly interesting. It had been thought for some time that salmonella organisms played a significant part in infantile diarrhoea in Australia. At the Royal Children's Hospital records of that group had been kept only during the past seven years, but they did show a constant stream of admissions, about 15% of all patients with diarrhoea being infected with salmonella. The patients in that group were admitted from all parts of Melbourne, but were fairly evenly distributed between the outer unsewered areas and the industrial areas; a few came from the middle suburbs. There were three patients from Camp Pell, and each was a baby who had been discharged only a few days earlier from the enteritis ward of the hospital. A most noticeable rise in admissions occurred during December, January and February.

In contrast to the position in the other two groups, a much higher percentage of salmonella patients came from small families living in standard accommodation where personal and household hygiene was excellent. The income level, on the whole, was high. In that group a smaller percentage of patients was known to have had possible contact with other patients suffering from diarrhoea. The patients fell into a slightly higher age group than those in the non-specific group. Of the 56 patients, only one baby, aged three weeks, was wholly breast-fed, and three babies, eight to nine months old, were partly breast-fed at the time of admission to hospital. A greater number of the mothers regularly attended infant welfare centres. The overall picture in relation to breast-feeding was not good. During the past year in the infant welfare centres it was found that about 47% of babies were still being breast-fed at three months of age and 33% at six months of age. In the present survey only 14% of babies under three months of age were wholly breast-fed at the time of admission to hospital, and up to the age of six months only 9%.

Of the babies who were fed on artificial feedings, a slightly smaller number were having cow's milk than were

having a commercial milk. Of all the homes 15% lacked either refrigerator or ice chest, and in these homes food-stuffs, including milk, were seldom kept in any place other than a cupboard. Half the homes had no fly wires of any description; very few homes had protection of all windows and doors. Flies in varying numbers were seen in 70% of homes, and in most homes mothers stated that flies were troublesome. In 35% of homes garbage tins were uncovered, and were often placed near the kitchen door.

Of the infants studied 40% either had never attended an infant welfare centre, or had attended no more than once or twice. Mothers gave various reasons for non-attendances. Approximately 50% were attending regularly when the child became ill. In contrast it was estimated that about 70% of babies in the community were receiving infant welfare centre care in 1953.

In conclusion, Miss Allan said that it would appear that study of the social background of infants with infective diarrhoea seemed to endorse the widely held belief that breast-feeding was a protective weapon against infective diarrhoea in infants. It revealed that the emergency housing areas of Camp Pell, Lorimer Street and Watsonia were trouble spots, and indicated that the rapid post-war uncontrolled spread of Melbourne had increased the importance of unsewered areas in relation to this disease. In addition, there was evidence that infective diarrhoea was not confined to the economically poorer classes, to those who lacked personal and household cleanliness, or to those who lived in substandard homes.

DR. H. E. WILLIAMS, in opening the discussion, said that Miss Allan had presented a comprehensive picture of the social background of a common illness. Criticisms which might be made were that the sample of 174 patients was, as a representative sample, too small, and that insufficient control infants were available. If those faults were allowed for, the survey was most informative. The family backgrounds had been studied meticulously, and the series covered a wide range in the population, not solely in the poorer industrial areas. On most occasions it was unnecessary to study the home environment exhaustively or to obtain bacteriological assistance to identify the source of infection. The survey made it obvious that infective diarrhoea in infancy was a preventable disease, if facilities were adequate, and the parents were reasonably well informed. It was significant that many infected infants came from good type families with adequate incomes and a high standard of hygiene, but living in unsewered areas. That fact was salutary to those responsible for town planning, sewerage, water and transport, *et cetera*. Dr. Williams said that it was obvious that breast-fed infants were much less liable to develop infective diarrhoea. Claims to the contrary by American workers were nonsensical. A most important problem was that of educating parents to care for their children. Many mothers did not have elementary knowledge of child welfare, and others had inadequate facilities. The infant welfare movement was a tremendous force, but many mothers did not attend centres. Dr. Williams concluded by saying that it was more important to concentrate on slum-clearance and the building of adequate houses than to expend money on large hospitals.

DR. P. GILBERT said that infant welfare centres were important, but even more important to the welfare of the child was the system, common in England, of public health nurses going into homes and instructing mothers. There were practical difficulties involved in infant welfare sisters going into homes. Instructions given by sisters in infant welfare centres frequently fell on barren soil.

DR. ROSE MUSHIN asked if there were data on the seasonal incidence of infective diarrhoea in industrial suburbs. Was it really a summer diarrhoea? Were there more instances of non-specific diarrhoea in winter?

Miss Jean Allan, in reply, said that it was difficult to determine seasonal incidence from infants included in the survey. They were drawn from one ward of fourteen cots and included children from institutions and country districts. A varying number in the ward were over two years old. They were not included in the survey. There appeared to be a seasonal rise in summer with salmonella and "non-specific" infections. Minor rises occurred during winter. Shigella infections occurred in epidemics, of which the worst in 1953 was in March.

DR. V. L. COLLINS said that Miss Allan's work demonstrated that many problems in the community had to be tackled in a similar manner. The medical profession must make its voice heard.

DR. NORMA KELSO said that she spoke as an infant welfare officer who worked in Camp Pell. She agreed that the

problem was largely one of education. Many mothers did not attend infant welfare centres, and it was difficult for the nursing sisters in charge of those centres to visit homes. Some mothers who did not attend health centres adopted a rather superior attitude, but the majority were too shiftless, and the latter group was found in Camp Pell. The solution to the problem might lie in education of girls before marriage, starting in schools. However, many teachers, obsessed by examination results, felt that time should not be wasted on "unessential subjects" like mothercraft. The subject was being dealt with thoroughly in some schools. Dr. Kelso expressed the opinion that some of the worst offenders in discontinuing breast-feeding were medical practitioners. There existed a mistaken idea that breast-feeding was difficult. Dr. Kelso said that she doubted whether the adoption of artificial feeding eased a mother's problem. Given reasonable home conditions and reasonably sized families, most mothers should be able to breast-feed their babies. Many young practitioners must accept the blame for discontinuing breast-feeding for mild illnesses like upper respiratory tract infections in infants.

Dr. H. McLORINAN said that most of Miss Allan's conclusions were well founded and informative, but he sounded a warning against drawing too drastic conclusions. The patients admitted to the Royal Children's Hospital might not be truly representative of Melbourne's children with infective diarrhoea, as they might include a high proportion of those from Camp Pell.

#### The Effect of Chloramphenicol in Salmonella and Non-Specific Enteritis of Infancy.

Dr. W. B. MACDONALD presented the results of a controlled therapeutic trial to determine the efficacy of chloramphenicol in the treatment of salmonella and non-specific enteritis of infancy. All the infants were less than two years old, had been ill less than one week, and were free from parenteral infection or feeding upset. None had been treated before admission to hospital. Treated and control infants were selected at random to eliminate bias, and were given the same general treatment of fluid, electrolytes and graded dried milk formulae. Treated infants received 120 milligrammes of chloramphenicol per kilogram of body weight daily for ten days.

Dr. Macdonald demonstrated tables, conclusively establishing that in the series of 25 treated and 26 control infants, chloramphenicol was ineffective in the treatment of salmonella enteritis, determined on both clinical and bacteriological criteria. The majority of infants were infected with *Salmonella typhimurium*. Dr. Macdonald said that the conclusions were so clearly established that statistical analysis was unnecessary. The results were to be published in detail at a later date in *Archives of Disease in Childhood*.

Dr. Macdonald then demonstrated the effect of chloramphenicol in a series of 26 treated infants and 21 controls with "non-specific" enteritis. The criteria of preselection were the same as for those infected with salmonella. Owing to the wide range of possible pathogens in this group, together with occasional accepted pathogens which had not been isolated by faecal culture, and the natural variability of reactions of the patients, the total number of 47 infants was insufficient to establish more than very tentative conclusions with respect to the effect of chloramphenicol and the type of organism causing the illness. However, when an average was taken over the four bacteriological subgroups, chloramphenicol appeared ineffective.

Dr. Macdonald mentioned that the results were at variance with those obtained recently in the United Kingdom by the Medical Research Council teams of investigators. Although that might be due to the paucity of suitable infants, the two conclusions were compatible if the possible different distribution of organisms in the British series was considered. Furthermore, in that series, parenteral infections were not excluded, and those might have responded more easily to chloramphenicol, with consequent lessening of diarrhoea.

Dr. Binet, of the Department of Statistics, University of Melbourne, had analysed the results in the present series, and two definite conclusions had been established. The first was that the odds were 20 to one in favour of asserting that the duration of the illness was less in the older infants. The second conclusion was that the odds were 100 to one in favour of asserting that delay in starting treatment lengthened the duration of the illness; the "treatment" in this instance referred to the general management common to both chloramphenicol-treated and control infants, and not to chloramphenicol therapy itself.

Dr. Macdonald said that the first conclusion was supported by the impressions of many observers. The second conclusion was very interesting, as the obvious corollary was that there was a 100 to one probability that general nursing, hydration therapy and the dietary routine used during the trial were effective in shortening the course of the illness. That was a much stronger probability than the most optimistic reports of the effect of chloramphenicol.

It was most important for clinicians to realize that the cornerstone in the treatment of infantile diarrhoea was the nursing, hydration therapy and diet, and not antibacterial measures, which were on the whole very disappointing except in the treatment of shigella infections.

Dr. HOWARD WILLIAMS said that the results of the investigation spoke for themselves. There was little to add. Preliminary observations for the twelve months preceding the investigation had justified the use of controls.

Dr. S. W. WILLIAMS agreed that fluid, electrolytes and diet were important. The infants were receiving very good medical and nursing care in hospital, but under less ideal conditions outside there might still be a place for antibiotics and sulphonamides. It was possible that diarrhoea prevented an effective absorption of chloramphenicol, and if the latter was given parenterally it might provide a higher plasma concentration within the range of that effective against salmonella *in vitro*.

Dr. W. B. Macdonald agreed with Dr. Williams that a more effective plasma concentration of chloramphenicol might be obtained by parenteral administration, but said that even though that reached levels to which salmonella was sensitive *in vitro*, it was uncertain that the bowel infection would be controlled.

Dr. J. W. PERRY said that the salmonella types in the trial were almost entirely *S. typhimurium*. It would appear from Dr. Macdonald's results that chloramphenicol was ineffective in the treatment of diarrhoea due to *S. typhimurium*, but it might be effective in the treatment of infections with some of the other 200 types.

Dr. W. B. Macdonald replied that a wide range of *in-vitro* tests of sensitivity of numerous types of salmonella to chloramphenicol had been carried out by McLean and co-workers. Most types had similar degrees of sensitivity.

Dr. T. D. HAGGER mentioned the fact that several infants were serologically positive to salmonella and shigella in the absence of a positive stool culture result. Would withholding chloramphenicol from those infants jeopardize their chance of recovery?

Dr. W. B. Macdonald, in reply, said that he believed that in the case of shigella infections, withholding chloramphenicol would adversely affect the recovery rate, but not in the case of salmonella infections. His own observations had shown that almost all infants with shigella infections, and most of those with salmonella infections, had diarrhoea with blood-stained stools, whereas the minority of those with non-specific infections had this feature. Some of the latter were undoubtedly due to infection with shigella or salmonella, in which the organism had not been cultured. The risk of a child with an undetected shigella infection being deprived of specific antibacterial treatment made it obligatory to give sulphonamides, chloramphenicol or some other antibiotic specific to dysentery to infants with severe blood-stained diarrhoea and blood-stained stools even when no shigella had been cultured.

Dr. J. A. FORBES criticized the absence of chloramphenicol plasma concentration estimations. However, he said that it was questionable whether plasma levels were indicative of the efficacy of the drug in bowel infections. He recalled two patients with typhoid fever who despite apparent adequate doses of chloramphenicol had inadequate plasma levels.

Dr. JOHN COLEBATCH said that the only means of testing adequately the efficacy of a drug was by means of a controlled trial as was done by Dr. Macdonald. Before any other drug was acclaimed or condemned for infantile diarrhoea it would need to be subjected to such a trial. It was evident that chloramphenicol, although effective in the treatment of dysentery, was not effective for salmonella infections, and not highly effective for "non-specific" diarrhoea. It was important that one should critically evaluate claims for the effects of drugs both in medical journals and in advertising brochures. Dr. Colebatch said that the general practitioner, more especially the country practitioner, must act on his clinical diagnosis and should use some drug if in doubt as to the causative organism.

Dr. W. B. Macdonald said that he quite agreed with Dr. Colebatch. The trial had been conducted in vastly different circumstances from those faced by a country practitioner.

Dr. H. McLORINAN said that Dr. Macdonald's conclusions were dogmatic, and had proved that chloramphenicol was ineffective in the treatment of salmonella enteritis in childhood. Some attempt should be made to find a method of obtaining an effective plasma level of the drug.

Dr. W. B. Macdonald said that the various criticisms were realistic, but the conclusions established by the trial under those existing circumstances were valid.

## Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

### ILLNESS ON A TRANSPORT.

[From White's "Journal of a Voyage to New South Wales".<sup>1</sup>]

18 July, 1787.

BEING informed that several of the marines and convicts on board the *Alexander* were suddenly taken ill, I immediately visited that ship and found that the illness complained of was occasioned by the bilge water which had by some means or other risen to such a height that the pannels of the cabin and the buttons on the clothes of the officers were turned nearly black by the noxious effluvia. When the hatches were taken off the stench was so powerful that it was impossible to stand over them. How it could have got to this height is very strange; for I well know that Captain Phillip gave strict orders (which orders I myself delivered) to the masters of the transports to pump the ships out daily in order to keep them sweet and wholesome; and it was added that if the ships did not make water enough for that purpose, they were to employ the convicts in throwing water into the well and pumping it out again until it became clear and untinged. The people's health however being endangered by the circumstance I found a representation upon the subject to Captain Phillip needful and accordingly went on board the *Sirius* for that purpose. Captain Phillip who on every occasion shows a great humanity and attention to the people, with the most obliging readiness sent Mr. King one of his lieutenants on board the *Alexander* with me in order to examine the state of the ship; charging him at the same time with the most positive and pointed instructions to the master of the ship instantly to set about sweetening and purifying her. This commission Mr. King executed with great propriety and expedition and by the directions he gave such effectual means were made use of that the evil was soon corrected; and not long after all the people who, suffering from the effects of it, were under Mr. Balmain my assistant's care, got quite rid of the complaint.

## Correspondence.

### A NOTE ON BRONCHIECTASIS.

SIR: There are still problems in the study of bronchiectasis that remain to be solved, and some aspects of the disease are still obscure. I would like to compliment Dr. Douglas on what has obviously been a careful and painstaking study ("A Note on Bronchiectasis", M. J. AUSTRALIA, June 12, 1954). However, I do not consider that the conclusions he has reached are justified by the facts published in his article.

It is true that in the great majority of cases of bronchiectasis, it is the presence of infection which determines symptoms, but it is not so in all cases. Everyone is familiar with those cases in which haemoptysis is the only symptom, and there is no infection present. Infection may have been present in the past to produce the bronchiectasis, but there is no active infection present to produce the symptoms in such cases.

The material reported shows that there can be infective changes present in the lung without bronchial dilatation. It may be possible for these changes to produce the symptoms of bronchiectasis, but there is no evidence in this article to prove that they do. In every one of the 15 cases listed there was at least one dilated bronchus present. Case VII was the closest to not having any, and in this case the posterior basal segment of the left lower lobe is shown as doubtful, so that one presumes that it could have been dilated. Accordingly, the symptoms in all cases could have been due to the dilated bronchi, and it is possible that the infective changes present played no part in their production. After all, infective changes are often present in the lung without producing the symptoms of bronchiectasis. Also it is well known that a very small area of dilatation can produce gross symptoms.

It is noted that in every case (where there is information available) in which the bronchi were dilated, they were also infected. So this series of specimens could support the statement quoted by Dr. Douglas from Marshall and Perry (1952) that symptoms depend on infection being superadded to bronchi which are already dilated.

The contribution which this article makes is to draw attention to the fact that there are different types of bronchiectasis that behave in a different manner.

In some there is crowding and generalized dilatation of bronchi, the dilatation usually being of the saccular type. In others the dilatation is patchy, segments of various lobes being involved, and it is often cylindrical in type. Both these groups of cases do well with physiotherapy, but the results of surgery are much more satisfactory in the former than in the latter.

Yours, etc.,

A. G. McMANIS.

201 Macquarie Street,  
Sydney,  
June 15, 1954.

### NATIONAL HEALTH (PHARMACEUTICAL BENEFITS) REGULATIONS.

SIR: In common with most general practitioners, we have always considered the Pensioners' Medical Scheme a timely and beneficial measure for this class of patient. The Pharmaceutical Benefits Scheme, also, has enabled practitioners to treat illness in the community without the worry of involving the patient in too great a financial burden. When they were originally instituted, these measures appeared greatly preferable to those proposed by the Chifsey Government, particularly as regards the freedom to prescribe, and in regard to the absence of harassing regulations.

The latest handbook of rules, received within the last few days, shows serious departures from this happy state of affairs, and if the trend is to continue, serious doubts will be raised as to the efficiency of the scheme, and many of the advantages which induced the medical profession to welcome it in the first place will be removed. The undersigned medical practitioners of this town have seriously considered whether the general practitioners of Australia might not be wiser to dissociate themselves from the scheme, if it is to become a burden instead of a help.

To give some examples, most practitioners have had their prescription forms printed in accordance with previous requirements, and we now find that the superscription is to be altered, and there is to be a greater insistence on exact size. What possible advantage can this give, and how can it increase the efficiency of the scheme? It bears the hall-mark of a bureaucratic exaction. Further, "Special and Double Supply" prescriptions no longer apply. This can be a source of great inconvenience, especially in the country, to patients who live long distances out. Considerations of age, infirmity and inclement weather have simply been disregarded. The option to "write to the Director-General" in each individual case is not likely to commend itself to the average practitioner; nor will the provision that written prescriptions must be supplied within twenty-four hours. We venture to say that this latter regulation may be looked on as stillborn.

Certain anomalies have always existed, but we have hitherto assumed that the scheme would be administered sympathetically. In the new regulations we note that they are not only perpetuated, but intensified. For example, certain drugs are restricted to certain conditions in which penicillin and sulphonamides fail to act. What of the patient with allergy or other type of intolerance, in whom these drugs cannot be tried? Or what of the patient who is unable to attend for injections, because of distance, or infirmity or

<sup>1</sup>From the original in the Mitchell Library, Sydney.

lack of transport—as often happens in the country? And with regard to urinary infections due to Gram-negative bacilli, what of the vast number of people in this country to whom no suitable facilities are available for making this determination? Further, in cases in which aureomycin is permitted to be administered, why is the only form suitable for administration to children not on the list?

In the case of penicillin, the amount permitted to be prescribed per patient of procaine penicillin aqueous suspension is 1,500,000 units, which is not sufficient for some patients receiving home treatment. In the case of the doctor's emergency list, the amount of 18,000,000 units is mentioned. It is not clear whether this is intended for a month's supply for use in the surgery. If so, it is grossly inadequate. If it is intended that this shall only be used for emergency calls, the result would be that the patient would have to be sent down with a prescription, involving two visits to the surgery for the patient, and for the doctor a vast amount of unnecessary writing. There are days when this could happen half a dozen times.

In the case of the Pensioners' Benefits it is noted that repeats have been cut to two, for mixtures and for powders for internal use. As these are very frequently used this seems to put an unfair burden on pensioners, who are usually old and sick, requiring them to attend more often than is necessary. We would also mention the increased cost of the extra visits made by the patients to the doctors.

We do not apologize for writing at some length—we doubt if even so we have exhausted all possible objections to the new regulations. The difficulties referred to are real and practical, and we have a strong suspicion that the general practitioners of Australia will require some explanation for this state of affairs, which seems to be based on the assumption that they are lacking in intelligence and integrity.

Yours, etc.,

Palla Street,  
Griffith,  
New South Wales,  
June 11, 1954.

A. E. W. BURRELL.  
G. OXENHAM.  
R. A. MCGREGOR.  
R. MCFADZEAN.  
J. GRAY.

SIR: I have just received the latest number of your journal and have been overwhelmed at the new series of regulations in connexion with the *Pharmaceutical Benefits Act*. Many of us feared when this was first introduced that we were placing ourselves in the hands of the bureaucrats. Why we have to change from "Pharmaceutical Benefits" to "N.H.S." and from "P.M.S." to "Pensioners' Benefit" I cannot understand—the pharmacists and doctors have been accustomed to one set-up, only to have to reverse our procedure, and alter our printed stationery, at the whim of someone sitting in an office chair.

Yours, etc.,

137 Macquarie Street,  
Sydney,  
Undated.

LINDSAY DEY.

#### VITAMIN B<sub>12</sub> IN CYANIDE POISONING.

SIR: The following communication has reached me by courtesy of Mr. C. W. Anderson, Chief Inspector of Pests and Diseases of the Australian Wheat Board:

Because Vitamin B<sub>12</sub> (Hydroxo-Cobalamin) reacts with Cyanides to produce Vitamin B<sub>12</sub> (Cyano-Cobalamin) in an apparently irreversible action in animals, Mushett et al. have investigated its potential beneficial influence in Cyanide poisoning.

Mice were poisoned with Potassium Cyanide, and when they were "apparently dead" (i.e., they showed neither respiration nor responsiveness to external stimuli) Vitamin B<sub>12</sub> was injected. The majority of mice reacted dramatically. Respiration frequently returned even before the entire dose was injected, and at the end of the injection many mice were able to walk about immediately.

After the injections, some of the cyanide appeared in the urine as thiocyanate, but the greatest proportion appeared as Vitamin B<sub>12</sub>.

The above information is contained in the August, 1953, issue of the Commonwealth of Australia, Department of Health, Pesticides Quarterly Supplement.

The work of Mushett et al. appears in the *Proceedings of the Society of Experimental Biology and Medicine*, 1952, pages 234-237: "Antidotal Efficacy of Vitamin B<sub>12</sub> (Hydroxo-Cobalamin) in Experimental Cyanide Poisoning", Charles Mushett et al.

In view of the recent happening in Melbourne, this information might be of general interest and the subject further investigated.

Yours, etc.,

12 Meadow Street,  
East St. Kilda,  
Victoria.  
June 10, 1954.

DOUGLAS G. RENTON, F.F.A.R.A.C.S.

#### DELAYED POST-OPERATIVE RECURARIZATION.

SIR: I was interested to read the account of "Delayed Post-Operative Recurarization" by R. A. Joske, P. Ebeling and R. H. Stanistreet. I would like to know what criteria were used to assess the patient's recovery from curarization at the completion of operation—whether, for example, intercostal breathing was present and also good jaw tone. The doses of "Flaxedil" the authors quote in Cases I and IV seem very large, especially in comparison with the dose of "Prostigmin" they use to produce recovery. In Case III a very large dose of "Flaxedil" is used with no "Prostigmin" at all. I cannot feel surprised that the patients were discovered post-operatively in a state of curarization, but am surprised that they were ever deemed, at the termination of operation, not to be so. It is possible that respiration was just adequate with the peripheral stimulating effect of a new and painful operation wound during removal of the patient from the operating table. When the patient was comfortable in bed, with a post-operative injection to dull his respiratory centre, it could easily become inadequate.

Yours, etc.,

Ballou Chambers,  
Wickham Terrace,  
Brisbane.  
June 15, 1954.

JOAN DUNN.

#### THE PRACTITIONER AND URGENT CALLS.

SIR: In *The Sydney Morning Herald* of June 9, 1954, the following paragraph occurs:

The tribunal is of the opinion that in cases of an urgent nature when a person has not been attended immediately prior to the making of arrangements for admission to hospital it is desirable that the attending doctor should proceed to the home of the patient after these arrangements have been made.

If this is a correct report, such a statement shows complete lack of common sense or appreciation of the conditions of country general practice. To follow this advice rigidly would lead to loss of life and unnecessary delay in the treatment of patients. If a nurse from a settlement fifteen miles away rings up to say that a baby boy, breast fed, of ten months, has been screaming and turning pale at intervals of twenty minutes, and has now passed some red jelly which looks like blood, what should I do? Arrange for the admission of the child and waste precious time travelling thirty miles while another patient has her baby in my absence, or apply the common sense so necessary to run a rural general practice and ask for the child to be brought in immediately for operation? Would it be relevant to ask if any of the gentlemen comprising the tribunal had ever been in general practice?

Yours, etc.,

398 Crown Street,  
Wollongong,  
New South Wales.  
June 10, 1954.

MALCOLM MCKINNON.

#### DANGEROUS DRUGS IN DISGUISE.

SIR: Today I found in the post a very elegant package containing twelve tablets. The accompanying brochure explained that each tablet contained, in addition to phenacetin (which was referred to as acetphenetidin) and caffeine, a third drug called phenyl-dimethyl-isopropylpyrazolone. I wonder how many of your readers know that this is another name for phenazone.

By the same mail came another advertisement (no samples) extolling the virtues of another product—an "anti-asthmatic". This time, one of the ingredients was described as phenylidimethyl pyrazolonum. I do not know for certain that this drug is phenazone or a closely allied drug, but I am rather suspicious.

Since, many years ago, amidopyrine and similar drugs, including phenazone, came under suspicion as possible causes of agranulocytosis, I, in common with very many physicians, have never prescribed phenazone.

The point of my letter is that, if manufacturing chemists insist on still including phenazone or any other potentially dangerous drug in their products, they should use the commonly used name, so that it would be impossible for anyone to prescribe any such drug unwittingly.

Yours, etc.,

R. K. RAE.

4 George Street,  
Hornsby,  
New South Wales.  
June 10, 1954.

#### WHAT SHOULD THE CANCER PATIENT BE TOLD?

SIR: Your editorial comment (June 12) on "What Should the Cancer Patient be Told?" is an excellent review of conflicting opinions on this important question. However, as it states no general principles the editorial fails to give any guidance to the medical reader who seeks in his journals just that guidance.

For there are certain definite principles commonly recognized and sanctioned by the natural law, namely:

1. In the great majority of cases it is unwise to tell a patient that he has cancer, as the psychiatric impact of the dread word is often disastrous to a sick person.

2. However, if he is in immediate danger of death, the physician should see that the patient is informed of this: (a) that he may make his peace with God, (b) that he may set his temporal affairs in order, in justice to his heirs et cetera.

Usually it is wise to impart the diagnosis to the next of kin, according to the latter's wishes. Legally it is possible for the physician to find himself up against the heirs, if the patient dies intestate through omission of the above duty (and conversely, in a famous case a doctor has been sued for heavy damages for giving a patient a wrong diagnosis of cancer, thereby causing him to dispose of his worldly assets).

Thus while there are sound reasons for avoiding the dread word "cancer" with a patient, we are bound in charity to ensure that his spiritual and temporal interests do not suffer through failure to warn him of the seriousness and probable outcome of his malady.

Yours, etc.,

DAVID B. PITT.

79 North Road,  
Oakleigh,  
Melbourne.  
June 16, 1954.

### The Royal Australasian College of Physicians.

#### SIXTEENTH ANNUAL MEETING.

THE sixteenth annual meeting of The Royal Australasian College of Physicians was held at Melbourne, Victoria, from May 26 to 29, 1954.

The Council of the College is at present constituted as follows: *President*: Dr. C. G. McDonald. *Vice-Presidents*: Dr. Ralph Wishaw, Dr. A. D. S. Whyte, M.C., Dr. Ian J. Wood, M.B.E. *Censor-in-Chief*: Dr. T. M. Greenaway. *Honorary Treasurer*: Dr. W. P. MacCallum, C.B.E., D.S.O., M.C., E.D. *Honorary Secretary*: Dr. H. Maynard Rennie. *Past President*: Sir Alexander Murphy, K.B., M.C. *Elected Councillors*: Sir Charles Blackburn, Kt., O.B.E., Dr. Clive Pitts, Dr. T. M. Greenaway, Dr. J. G. Hayden, C.B.E., E.D., Dr. A. Homes & Court, Dr. F. Ray Hone, Dr. Bruce Hunt, M.B.E., Dr. J. A. D. Iverach, Dr. Guy Lendon, Dr. K. B. Noad, Dr. E. G. Sayers, Dr. S. A. Smith, Dr. Allan S. Walker, Dr. Ian J. Wood, M.B.E., Dr. J. J. Billings, Dr. D. S. Stuckey, Dr. J. Eric Clarke.

At a meeting of the General Body of Fellows, Professor H. N. Robson was elected to Fellowship of the College under the special provisions of Article 44, which permits of the election to Fellowship of persons who have distinguished themselves in any branch of medical science or internal medicine. The following members were elected to Fellowship: Dr. P. L. Bidstrup (United Kingdom); Dr. C. R. Furner, Dr. S. J. M. Goulston, Dr. K. S. Harrison, Dr. Mary Heseltine, Dr. James Isbister, Dr. M. R. Joseph, Dr. V. J. McGovern, Professor F. R. Magarey, Dr. S. Ralph Reader and Dr. S. E. L. Stening (New South Wales); Dr. D. G. Duffy, Dr. H. B. Kay, Dr. P. J. Parsons, Dr. W. McI. Rose, Dr. H. J. B. Stephens and Dr. Marion Wanliss (Victoria); Dr. J. M. Bonnin and Dr. R. F. West (South Australia); Dr. M. H. Aiken and Dr. C. G. Riley (New Zealand).

The following candidates who were successful at an examination for membership held in Australia in April-May, 1954, were admitted by Council to membership of the College: Dr. C. R. Boughton and Dr. J. C. Quoye (New South Wales); Dr. G. H. Neilson and Dr. J. J. Sullivan (Queensland); Dr. S. G. Anderson, Dr. V. G. Bristow, Dr. K. G. Chatfield, Dr. A. Fisher, Dr. J. R. Kelly, Dr. W. R. Kingston, Dr. B. L. Marks, Dr. R. Mottram and Dr. M. J. Robinson (Victoria); Dr. A. K. Cohen (South Australia); Dr. H. R. Elphick and Dr. O. B. Tofler (Western Australia).

The following candidates who were successful at an examination for membership held in New Zealand in February, 1954, were also admitted by Council to membership of the College: Dr. R. H. Caughey, Dr. H. K. Ibbertson, Dr. J. K. Laing, Dr. T. V. O'Donnell and Dr. I. A. M. Prior (New Zealand).

#### ORDINARY MEETING, 1954.

THE ordinary meeting of the College in 1954 will take place at Sydney from October 13 to 16.

#### RESEARCH FUND.

THE College invites medical practitioners to submit applications from the Research Fund of the College before September 15, 1954. Applications should be made on the prescribed form, which may be obtained from the Honorary Secretary of the College at 145 Macquarie Street, Sydney.

### Naval, Military and Air Force.

#### APPOINTMENTS.

THE undermentioned appointments, changes et cetera have been promulgated in the *Commonwealth of Australia Gazette*, Number 35, of June 3, 1954.

#### ROYAL AUSTRALIAN AIR FORCE.

##### Permanent Air Force: Medical Branch.

The following Flight Lieutenants are granted the acting rank of Squadron Leader, 15th April, 1954: A. D. Litchfield (024304), P. A. O'Brien (035952).

The probationary appointment of Pilot Officer L. T. C. West (041923) is confirmed and he is promoted to the rank of Flying Officer, 30th March, 1954.

The undermentioned appointments, changes et cetera have been promulgated in the *Commonwealth of Australia Gazette*, Number 36, of June 10, 1954.

#### AUSTRALIAN MILITARY FORCES.

##### Australian Regular Army.

##### Royal Australian Army Medical Corps.

The Short Service Commission granted to 3/40113 Captain P. J. C. Stretton is extended until 23rd April, 1954.

3/40113 Captain P. J. C. Stretton is transferred to the Reserve of Officers (Royal Australian Army Medical Corps) (Medical) (3rd Military District), 24th April, 1954.

The Short Service Commission granted to 2/40153 Captain R. H. Higham is extended until 23rd April, 1954.

2/40153 Captain R. H. Higham is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (2nd Military District), 24th April, 1954.

#### Citizen Military Forces.

##### Northern Command: First Military District.

**Royal Australian Army Medical Corps (Medical).**—The following officers are seconded whilst undergoing post-graduate studies in the United Kingdom: Captains 1/39132 I. S. Holle, 10th February, 1954, and 1/39130 P. J. F. Grant, 4th May, 1953.

**Royal Australian Army Medical Corps (Medical).**—1/39173 Honorary Captain H. R. West is appointed from the Reserve of Officers, and to be Captain (provisionally), 23rd April, 1954. To be Captain (provisionally), 3rd May, 1954: 1/62657 Ronald Arthur Rimington.

##### Eastern Command: Second Military District.

**Royal Australian Army Medical Corps (Medical).**—To be Captain (provisionally), 14th April, 1954: 2/127888 Andrew Gordon Gregory Bennett.

##### Southern Command: Third Military District.

**Royal Australian Army Medical Corps (Medical).**—3/101012 Major C. F. Macdonald is seconded whilst undergoing post-graduate studies in the United Kingdom, 5th February, 1954. 3/52176 Captain (provisionally) J. A. Forbes relinquishes the temporary rank of Major and the provisional rank of Captain, and is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (3rd Military District), and is granted the honorary rank of Captain, 14th November, 1953. 3/73277 Captain J. W. Bennett is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (3rd Military District), 17th January, 1954.

##### Central Command: Fourth Military District.

**Royal Australian Army Medical Corps (Medical).**—4/31918 Captain (provisionally) C. S. Kneebone relinquishes the provisional rank of Captain and is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (4th Military District) in the honorary rank of Captain, 21st March, 1954. To be Captain (provisionally), 12th April, 1954: 4/32049 John Byrne Murchland.

**Royal Australian Army Medical Corps (Medical).**—4/32018 Captain B. L. Cornish is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (4th Military District), 1st April, 1954.

##### Western Command: Fifth Military District.

**Royal Australian Army Medical Corps (Medical).**—The provisional rank of 5/26514 Captain R. Paton is confirmed. 5/32249 Major A. A. Merritt is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (5th Military District), 9th April, 1954.

#### Reserve Citizen Military Forces.

##### Royal Australian Army Medical Corps.

**First Military District.**—To be Honorary Captains: Timothy Colville Barrett, 26th March, 1954; Duncan Robertson and William Sydney Egerton, 29th March, 1954; Barry Geoffrey Downs, 23rd April, 1954, and James Stuart Dixon and John Roy Cox, 26th April, 1954.

**Second Military District.**—To be Honorary Captain, 5th April, 1954: Edward Henry Holland. The resignation of the following officers of their commissions are accepted: Honorary Captain E. L. Fischer, 10th March, 1954, and Honorary Major M. Sterling-Levis, 23rd March, 1954.

**Third Military District.**—To be Honorary Captains: Peter Robin Macneil, 28th February, 1954, and Norman John Royal, 1st March, 1954.

##### ROYAL AUSTRALIAN AIR FORCE.

##### Air Force Reserve: Medical Branch.

The following are appointed to commissions, 1st April, 1954, with the rank of Flight Lieutenant: Kenneth Daniel Hatfield (268030), Brian Michael Dwyer (268031), Henry James Mitchell (268032).

The provisional appointment of the following Pilot Officers is confirmed and they are promoted to the rank of Flight Lieutenant, 31st March, 1954: R. C. Bennett (04713), I. N. Broadbent (04739), J. R. Lawrence (04720).

## Obituary.

### JAMES CALVERT SPENCE.

We are indebted to Professor Lorimer Dods for the following appreciation of the late James Calvert Spence.

Occasionally there appears a man with an indefinable quality which depends not on worldly success or professional ability, but on a subtle combination of ability, personality and devotion to certain ideals—a quality which sharply distinguishes him from his fellow men. Such a man was James Calvert Spence, Professor of Child Health in the University of Durham, who died on May 25, 1954, in his own beloved and native Newcastle-upon-Tyne.

James Spence was educated in Northumbria, hesitated between architecture and journalism in his choice of a profession, finally chose medicine, and graduated with honours from the University of Durham in 1914. A natural athlete with a special love of mountaineering and the apparently impossible climb, he played football for his university and had a gay zest for living which brought him many friends. A few months after graduation he volunteered for the army, served with distinction on Gallipoli and in France, and was awarded the Military Cross and bar.

His first close contact with the practice of paediatrics came soon after the armistice, when he was appointed to the resident medical staff of the Hospital for Sick Children, Great Ormond Street. A year or two later he was awarded the John and Temple research fellowship at Saint Thomas's Hospital, and in the middle 1920's he returned to his own city as "chemical pathologist and medical registrar" to the Royal Victoria Infirmary. In 1927 a Rockefeller Fellowship took him to the Johns Hopkins Hospital, Baltimore, where he spent a very happy year and made a number of lifelong friends. On his return to Newcastle, he was appointed to the honorary medical staff of the Royal Victoria Infirmary and the Newcastle General Hospital and commenced practice as a consulting physician.

It was during the next few years that his paediatric interests became apparent in his studies of the prevention and treatment of rickets carried out for the Medical Research Council of Great Britain, in his investigation into the health and nutrition of Newcastle children, and in the report which he and his associates prepared on the causes of infant mortality in their city.

The outstanding achievement of this period of James Spence's life was his establishment of "The Newcastle Babies' Hospital" in an early Victorian terrace house, where sick infants were nursed and cared for by their mothers in individual rooms, under the supervision of a small trained nursing staff. It was here, in this very small, improvised hospital, in the early 1920's, that he first established the obvious value to the mother and her sick child of this "rooming-in" mechanism. Writing of this "babies' hospital", which was his special pride and joy, Spence pointed out that "the mother needs little or no off-duty time, because the sleep requirements of a mother fall near to zero when her own child is acutely ill. She feeds and tends the child, she keeps it in its most comfortable posture on its pillow or her own knee" and she provides that maternal love and security which are essential for the child. He also applied these same concepts to the wards of the Maternity Hospital in his city, where he established the principle that the baby should be kept beside the mother's bed rather than in a separate ward. In his Charles West lecture on "The Care of Children in Hospital" (Royal College of Physicians, 1946) he caricatured the maternity hospital which represents the hygienist's dream of perfection, where mothers lie in rows of immaculate beds against sterile walls, while their infants lie in cots set in rows in another room, "out of earshot, out of sight but not out of mind . . . at regular intervals the infants are placed on a trolley, wheeled along the corridor and with the ringing of a bell which announces that milking time is at hand, they are delivered to the ward in which the mothers wait. Milking time over, the babies are re-embarked for their nursery".

In 1942 James Spence was appointed as the first Nuffield Professor of Child Health in the University of Durham and established a department which very quickly became one of the most famous and happy paediatric centres in the world.

In 1947, after much careful planning, he and his staff commenced their "thousand family survey"—a long-term observation of 1000 infants who were born in Newcastle during May and June of that year. This survey had as its objective the study of these infants, their disorders and their

illnesses against the natural background of the homes and the families in which they lived. Spence argued that observing the child and his disorders against the social, economic and emotional background of the home and the family was like watching a play from the wings of a theatre rather than through the narrow blinkers of hospital practice. He also maintained that an intelligent community which really wanted to improve its health would put its best doctors into general practice and give them sufficient leisure to study health and disease in the family and the home. The detailed reports of the first five years of this very significant "thousand family" survey were completed last year.

For those of us who have had the privilege of watching him at work in his own department, probably the most inspiring memory is that of James Spence demonstrating to a small group of two or three silent and most appreciative students something of the art of consultation and the art of "giving explanation and advice which is the purpose of a consultation"—teaching these students by personal precept something of the intimacy, the courtesy, the sympathy and the understanding which are required on such occasions. These special sessions were held in the out-patient department solely for the purpose of demonstrating this art and technique of consultation to students, who were warned beforehand that they must watch and listen in complete silence with as much self-effacement as possible.

Some of us have also had the pleasure of listening to James Spence planning a study of the natural pattern of some disease with his devoted team, to whom he was an unceasing inspiration. To discussions of this type he brought a combination of vivid imagination, clear and incisive thinking, and a delightful sense of humour which managed to brighten the most sombre session. On such occasions, the child and his possible reactions to any proposed investigations always received first consideration, for as Spence once pointed out, there is no tribunal which passes judgement on what is malpractice in the investigation of the child except "that faculty which distinguishes right from wrong and which we may still call 'conscience'".

In 1948 he spent several months in Australia as a visiting lecturer—an extraordinarily significant visit which brought a new and exciting philosophy to those who listened to him—and was responsible for a reincarnation of paediatrics in this country. The memory of this most stimulating visit will live for a long time in this country, particularly in the minds of the many young medical men and women who had the privilege of meeting and talking with him or listening to his lectures, which were delivered with a delightful informality that suggested the intimacy of a personal conversation.

Before coming to Australia he had talked with some of us about the question of forming an Australian Paediatric Association, and this association, which has since been established, owes a great deal to his sound advice and guidance over the past five years.

In 1950 he received a knighthood for his outstanding contributions to paediatrics, an honour which brought great pleasure to his numerous friends and admirers in many countries. While in Australia he was awarded the honorary degree of doctor of science in the University of Western Australia, and the following year the honorary degree of doctor of laws was conferred on him by the University of Cincinnati. He was a foundation member of the British Paediatric Association, a leading spirit of this association for twenty-five years and its president in 1950. His able and enthusiastic service on many national committees such as the Goodenough Committee of the Royal College of Physicians, the University Grants Committee and the Medical Research Council of Great Britain significantly influenced the pattern of medical education and research and the design of hospital policy in Great Britain. As a special compliment to his ability, as a councillor, he was recently awarded the rare distinction of being elected to the Medical Research Council of Great Britain for a second term of office.

For the greater part of a year before his death James Spence knew that he was suffering from an incurable disease. Ill as he was, he carried on with his usual work, continued to take a very active interest in the affairs and plans of his department and remained a light-hearted companion to his family, his friends and his staff. It was during this period that he wrote to a friend: "My serenity surprises me . . . an unexpected contentment has settled on me."

There are men of great ability and sincerity, men who are outstanding teachers, men who have something of both the priest and the prophet in their nature, men of wide culture, vivid imagination and broad vision. James Spence was all these things and something more, for he was endowed with a great personal charm and a warm spirit of affection, which endeared him to his countless friends and disciples who now carry his memory in their hearts and minds.

## Congress Notes.

### AUSTRALASIAN MEDICAL CONGRESS (BRITISH MEDICAL ASSOCIATION).

THE Executive Committee of the Australasian Medical Congress (British Medical Association), Ninth Session, to be held at Sydney from August 20 to 27, 1955, has forwarded the following notes for publication.

Application forms for membership of the Congress are available from the Honorary Local Secretary of Congress in each State, namely: *New South Wales*: Dr. M. S. Alexander, 135 Macquarie Street, Sydney; *Victoria*: Dr. C. H. Dickson, Medical Society Hall, 426 Albert Street, East Melbourne, C.2; *Queensland*: Dr. D. A. Henderson, Ballou Chambers, Wickham Terrace, Brisbane, B.17; *South Australia*: Dr. L. Bonnin, 63 Palmer Place, North Adelaide; *Western Australia*: Dr. S. E. Craig, 7 Malcolm Street, Perth; *Tasmania*: Dr. K. S. Millingen, 178 Macquarie Street, Hobart.

#### Scientific Papers.

Members and intending members of Congress who desire to present papers to the meetings of Sections are advised that the Executive Committee has made the following decisions:

1. Offers of papers will be received by the Honorary Secretaries of Sections (see appended list) until March 31, 1955, and authors must indicate at least the title of the proposed paper with a précis of its subject if a completed paper is not submitted.
2. Intending speakers will be notified not later than April 30, 1955, whether their offer of a paper has been accepted or rejected.
3. Three copies, in final form, of papers accepted (in addition to the author's copy), typed in double spacing on one side of the paper only, complete with illustrations, together with a note of visual aid requirements, must be in the hands of the appropriate Secretary of Section by June 30, 1955. One copy will be for the Chairman of the meeting at which the paper is to be presented, one for the Editor of THE MEDICAL JOURNAL OF AUSTRALIA and one for the lay Press liaison officer.

Under the rules of the Congress, no paper can be taken as read and, unless it is read, does not form part of the proceedings of Congress.

#### Honorary Secretaries of Sections.

Honorary Secretaries of Sections are as follows: *Anæsthesia*, Dr. P. L. Jobson; *Dermatology*, Dr. M. Hayvatt; *History of Medicine*, Dr. A. M. McIntosh; *Medicine and Experimental Medicine*, Dr. K. S. Harrison; *Naval, Military and Air Force Medicine and Surgery*, Dr. J. F. C. Cobley; *Neurology and Psychiatry*, Dr. I. G. Simpson; *Obstetrics and Gynaecology*, Dr. F. A. Bellingham; *Ophthalmology*, Dr. E. J. Donaldson; *Orthopedics*, Dr. A. I. Rhydderch; *Oto-Rhino-Laryngology*, Dr. T. H. O'Donnell; *Pathology, Bacteriology, Biochemistry and Forensic Medicine*, Dr. A. E. Gatenby; *Pædiatrics*, Dr. S. E. J. Robertson; *Public Health and Industrial Medicine*, Dr. R. T. C. Hughes; *Radiology and Radiotherapy*, Dr. D. B. Wightman; *Rehabilitation and Physical Medicine*, Dr. B. G. Wade; *Surgery*, Dr. A. C. R. Sharp; *Tropical Medicine*, Dr. C. J. N. Leleu.

All correspondence to Honorary Secretaries of Sections should be addressed to 135 Macquarie Street, Sydney, New South Wales.

#### Presidents of Sections.

Presidents of Sections are as follows: *Anæsthesia*, Dr. H. J. Daly, New South Wales; *Dermatology*, Dr. W. C. T. Upton, South Australia; *History of Medicine*, Dr. C. Craig, Tasmania; *Medicine and Experimental Medicine*, Dr. W. W. S. Johnston, Victoria; *Naval, Military and Air Force Medicine and Surgery*, Air Vice-Marshal E. A. Daley, Victoria; *Neurology and Psychiatry*, Dr. A. J. M. Sinclair, Victoria; *Obstetrics and Gynaecology*, Dr. G. Simpson, Victoria; *Ophthalmology*, Dr. A. F. E. Chaffer, New South Wales; *Orthopedics*, Dr. E. F. West, South Australia; *Oto-Rhino-Laryngology*, Dr. A. Kenneth Green, Queensland; *Pathology, Bacteriology, Biochemistry and Forensic Medicine*, Dr. A. H. Tebbutt, New South Wales; *Pædiatrics*, Dr. Kate I. Campbell, Victoria; *Public Health and Industrial Medicine*, Dr. H. M. L. Murray, Tasmania; *Radiology and Radiotherapy*, Dr. B. L. W. Clarke, Queensland; *Rehabilitation and Physical*

Medicine, Dr. C. W. Anderson, Western Australia; Surgery, Dr. Alan H. Lendon, South Australia; Tropical Medicine, Professor A. H. Baldwin, New South Wales.

## University Intelligence.

### UNIVERSITY OF MELBOURNE.

THE twentieth Halford Oration will be delivered by Professor Sir Howard Florey in the Public Lecture Theatre, University of Melbourne, at 8.15 p.m. on July 29, 1954. The subject will be "The Possible Relationship of Lipoids to Atherosclerosis". This lecture is open to all members of the medical profession. Entry will be free and without ticket.

## Post-Graduate Work.

### THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

#### Annual Subscription Course.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that Mr. A. Lawrence Abel, M.S., F.R.C.S., Senior Surgeon, Princess Beatrice Hospital and Gordon Hospital, and Surgeon, Royal Cancer Hospital, London, and Guest Professor to The Royal North Shore Hospital of Sydney, will give the following lecture in the Stawell Hall, 145 Macquarie Street, Sydney, at 3.15 p.m. on Thursday, August 12, 1954: "The Present Position of the Cancer Problem." This lecture is included in the annual subscription course by arrangement with The Royal North Shore Hospital of Sydney and in conjunction with the State Committee of the Royal Australasian College of Surgeons.

### Lecture at Balmoral Naval Hospital.

The Post-Graduate Committee in Medicine in the University of Sydney announces that Dr. Eric Goulston will give a lecture on "Acute Intestinal Obstruction" on Tuesday, August 10, 1954, at 2 p.m. Patients will be shown after the lecture. All members of the medical profession are invited to attend.

## Medical Prizes.

### THE SHORNEY PRIZE: A CORRECTION.

THE Registrar of the University of Adelaide asks us to announce that, owing to an oversight, the notice concerning the Shorney Prize which was submitted for publication in this journal (see the issue of June 5, 1954, at page 383) stated that the prize would be offered for the fifth time in 1955 and would be for work in diseases of the ear, nose and throat. However, as a prize is to be offered for work in that subject in 1954, the prize is to be offered for the sixth time in 1955, and will be for work in ophthalmology. The relevant clauses of the Statute governing the prize were published in the previous notice. Applications should be sent to the Registrar of the University of Adelaide.

## Notice.

### SECTION OF PREVENTIVE MEDICINE, VICTORIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION.

THE next meeting of the Section of Preventive Medicine of the Victorian Branch of the British Medical Association will be held in the Medical Society Hall, 426 Albert Street, East Melbourne, on Thursday, July 8, 1954, at 4.30 p.m. Dr. Donald M. McLean, of the Walter and Eliza Hall

### DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED JUNE 12, 1954.<sup>1</sup>

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism .. ..	7(7)	4(4)	4(1)	..	..	..	..	..	15
Amoebiasis .. ..	..	..	..	..	..	..	..	..	..
Ancylostomiasis .. ..	..	..	..	..	..	..	6	..	6
Anthrax .. ..	..	..	..	..	..	..	..	..	..
Bilharziasis .. ..	..	..	..	..	..	..	..	..	..
Brucellosis .. ..	..	..	..	..	1	..	..	..	1
Cholera .. ..	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus) .. ..	2(2)	..	..	..	..	..	..	..	2
Dengue .. ..	..	..	..	..	..	..	..	..	..
Diarrhoea (Infantile) .. ..	3(1)	11(11)	1(1)	..	..	..	..	..	15
Diphtheria .. ..	30(20)	3(3)	2(1)	..	..	..	..	..	35
Dysentery (Bacillary) .. ..	..	4(4)	1(1)	..	2	..	..	..	7
Encephalitis .. ..	1(1)	1	..	..	..	..	..	..	2
Filariasis .. ..	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice .. ..	..	..	..	..	..	..	..	..	..
Hydatid .. ..	..	..	..	..	..	..	..	..	..
Infective Hepatitis .. ..	26(10)	18(6)	..	..	2(2)	..	..	..	46
Lead Poisoning .. ..	..	..	..	..	..	..	..	..	..
Leprosy .. ..	..	..	..	..	..	..	..	..	..
Leptospirosis .. ..	..	..	..	..	..	..	..	..	..
Malaria .. ..	..	..	..	..	1(1)	..	..	..	1
Meningococcal Infection .. ..	5(4)	5(3)	1(1)	1	1	..	..	..	13
Ophthalmia .. ..	..	..	..	..	..	..	..	..	..
Ornithosis .. ..	..	..	..	..	..	..	..	..	..
Paratyphoid .. ..	1	..	..	1(1)	..	..	..	..	2
Plague .. ..	..	..	..	..	..	..	..	..	..
Pollomyelitis .. ..	8(1)	8(3)	3(1)	4(3)	0(1)	..	..	..	20
Puerperal Fever .. ..	1(1)	..	..	..	..	..	..	..	1
Rubella .. ..	..	5(4)	..	..	0(4)	..	..	..	11
Salmonella Infection .. ..	..	..	..	..	1	1	..	..	46
Scarlet Fever .. ..	18(7)	25(20)	2(2)	8(3)	1	..	..	..	46
Smallpox .. ..	..	..	..	..	..	..	..	..	..
Tetanus .. ..	..	..	1(1)	..	..	..	..	..	1
Trachoma .. ..	..	..	..	..	1	..	..	..	1
Trichinosis .. ..	..	..	..	..	..	..	..	..	..
Tuberculosis .. ..	32(23)	23(16)	36(29)	4(3)	3(3)	4(1)	..	..	102
Typhoid Fever .. ..	..	1	..	..	..	..	..	..	1
Typhus (Flea-, Mite- and Tick-borne) .. ..	..	..	..	..	2(2)	..	..	..	2
Typhus (Louse-borne) .. ..	..	..	..	..	..	..	..	..	..
Yellow Fever .. ..	..	..	..	..	..	..	..	..	..

<sup>1</sup> Figures in parentheses are those for the metropolitan area.

Institute of Medical Research, will give an address entitled "Influenza, 1954". Dr. McLean has been carrying out the major portion of the work on influenza at the Hall Institute this year. All members of the Branch are invited to be present.

## Public Health.

The following notice has appeared in the *Queensland Government Gazette*, Number 63, June 19, 1954:

His Excellency the Governor, with the advice of the Executive Council, has, in pursuance of the provisions of *The Health Acts, 1937-1945*, been pleased to approve of the following Regulations made by the Director-General of Health and Medical Services: "The Food and Drug Regulations of 1939" are hereby amended as follows:

The following Regulation (75A) is inserted after Regulation 75 of the said Regulation, namely:

### *Mercurous Chloride.*

75A. No person, other than upon the written prescription of a medical practitioner, shall sell any teething powder, soothing powder, infant's powder, or similar preparation containing mercurous chloride for internal use by children under the age of five years.

A. FRYBERG,  
Director-General of Health and  
Medical Services.

## Australian Medical Board Proceedings.

### NEW SOUTH WALES.

The following have been registered, pursuant to the provisions of the *Medical Practitioners Act, 1938-1950*, as duly qualified medical practitioners: Brotherton, James, M.B., B.S., 1952 (Univ. Durham); Edwards, Richard Edward Evan, M.B., B.S., 1947 (Univ. Queensland).

The following additional qualifications have been registered: Green, Leonard (M.B., B.S., 1947, Univ. Sydney), M.C.R.A., 1953, D.M.R.D., R.C.P. and S. (England), 1953; Kenny, Rawdon Hamilton (M.B., B.S., 1928, M.S., 1941, D.D.R., 1953, Univ. Sydney), M.C.R.A., 1953; Kerridge, Gordon (M.B., B.S., 1943, Univ. Sydney), F.R.C.S. (Edinburgh), 1953.

The following notification is published in the *New South Wales Government Gazette*, Number 91, June 11, 1954:

It is hereby notified that the name of George Basil Goswell, M.B., B.S., 1942, Univ. Sydney, has been removed from the Register of Medical Practitioners for New South Wales by order of the Disciplinary Tribunal.

## Nominations and Elections.

The undermentioned has applied for election as a member of the Victorian Branch of the British Medical Association:

Sugerman, David—Alexander, M.B., B.S., 1953 (Univ. Sydney), Royal Melbourne Hospital, Parkville.

The undermentioned have been elected as members of the New South Wales Branch of the British Medical Association: Carter, Peter Geoffrey, M.B., B.S., 1954 (Univ. Sydney); Gengos, Don Constantine, M.B., B.S., 1954 (Univ. Sydney); Harris, Michael James, M.B., B.S., 1954 (Univ. Sydney); Leong, Leonard Joseph Almone, provisional registration, M.B., B.S., 1954 (Univ. Sydney); Lowe, Alice Marie, M.B., B.S., 1954 (Univ. Sydney); McMillan, Bruce, provisional registration, M.B., B.S., 1954 (Univ. Sydney); Newlands, John Stuart, M.B., B.S., 1954 (Univ. Sydney); Nolan, Kenneth Ernest, provisional registration, M.B., B.S., 1954 (Univ. Sydney); Nordon, Jeanette Ilse, provisional registration, M.B., B.S., 1954 (Univ. Sydney); Phillip, George Blackmore, provisional registration, M.B., B.S., 1954 (Univ. Sydney); Searle, Alan William, provisional registration, M.B., B.S.,

1954 (Univ. Sydney); Treloar, Brian Tremayne, provisional registration, M.B., B.S., 1954 (Univ. Sydney); Vane, Amoury Arthur Joseph de Courcy, provisional registration, M.B., B.S., 1954 (Univ. Sydney); Wajeman, Maurice, provisional registration, M.B., B.S., 1954 (Univ. Sydney); Corrigan, Alfred Brian, M.B., B.S., 1953 (Univ. Sydney); Jane, Elizabeth Rae, M.B., B.S., 1953 (Univ. Sydney); Jones, John William Howard, M.B., B.S., 1953 (Univ. Sydney); Nesztel, Paul John David, M.B., B.S., 1953 (Univ. Sydney); Guyot, John Raymond Blee, M.B., B.S., 1952 (Univ. Sydney); Law, David John, M.B., B.S., 1950 (Univ. Sydney); Masters, Harold Elliott, M.B., B.S., 1952 (Univ. Sydney).

## Deaths.

The following deaths have been announced:

WILTON.—Alexander Cockburn Wilton, on June 6, 1954, at Clarendon, South Australia.

LINES.—David Henry Edward, on June 12, 1954, at Hobart.

## Diary for the Month.

JULY 6.—New South Wales Branch, B.M.A.: Council Quarterly.  
JULY 7.—Western Australian Branch, B.M.A.: Council Meeting.  
JULY 7.—Victorian Branch, B.M.A.: Clinical Meeting.  
JULY 9.—Queensland Branch, B.M.A.: Council Meeting.  
JULY 13.—New South Wales Branch, B.M.A.: Organization and Science Committee.

## Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

*New South Wales Branch* (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

*Queensland Branch* (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

*South Australian Branch* (Honorary Secretary, 178 North Terrace, Adelaide): All Contract Practice appointments in South Australia.

*Western Australian Branch* (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

*Tasmanian*: Part-time specialist appointments for the north-west coast of Tasmania.

## Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

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